DISSERTATION ON

A CORRELATIVE STUDY OF AUTOMATED PERIMETRY AND OPTICAL COHERENCE TOMOGRAPHY IN GLAUCOMA

Submitted in partial fulfillment of requirements of

M.S.OPHTHALMOLOGY

BRANCH – III

REGIONAL INSTITUTE OF OPHTHALMOLOGY
MADRAS MEDICAL COLLEGE, CHENNAI- 600 003.

THE TAMIL NADU DR.M.G.R.MEDICAL UNIVERSITY,

CHENNAI

APRIL 2015

CERTIFICATE

This is to certify that the dissertation titled, **"A CORRELATIVE STUDY OF AUTOMATED PERIMETRY AND OPTICAL COHERENCE TOMOGRAPHY IN GLAUCOMA"** is a bonafide record of the research work done by DR. J.JAYALATHA, post graduate in the Regional institute of Ophthalmology & Government Ophthalmic Hospital, Madras Medical Collage and Research Institute, Chennai - 03, submitted in partial fulfillment of the regulations laid down by the Tamil Nadu Dr. M.G.R. Medical University, Chennai for the award of M.S. Ophthalmology Branch III, Under my guidance and supervision during the academic years 2013-2015.

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DECLARATION BY THE CANDIDATE

I hereby declare this dissertation entitled “a correlative study of automated perimetry and optical coherence tomography in glaucoma” is a bonafide and genuine research work carried out by me under the guidance of Prof.Dr.Waheeda Nazir and Prof.Dr.M.R.Chitra.

DATE:

PLACE: Dr.J.JAYALATHA

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INSTITUTIONAL ETHICS COMMITTEE
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CERTIFICATE OF APPROVAL

To
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Dear Dr.J.Jayalatha,

The Institutional Ethics Committee of Madras Medical College, reviewed and discussed your application of the proposal entitled **"A CORRELATIVE STUDY OF AUTOMATED PERIMETRY AND OPTICAL COHERANCE TOMOGRAPHY IN GLAUCOMA"** No.48062014

The following members of Ethics Committee were present in the meeting held on 03.06.2014 conducted at Madras Medical College, Chennai -3.

1.	Dr. C. Rajendran, M.D.	-- Chairperson
2.	Dr. R. Vimala, M.D., Dean, MMC, Ch-3.	-- Deputy Chair Person
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11.	Thiru. S. Govindasamy, BABL, High Court, Chennai-1.	-- Lawyer
12.	Tmt. Arnold Saulina, MA MSW	-- Social Scientist

We approved the proposal to be conducted in its presented form.

Sd / Chariman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patient's information / informed consent and asks to be provided a copy of the final report.

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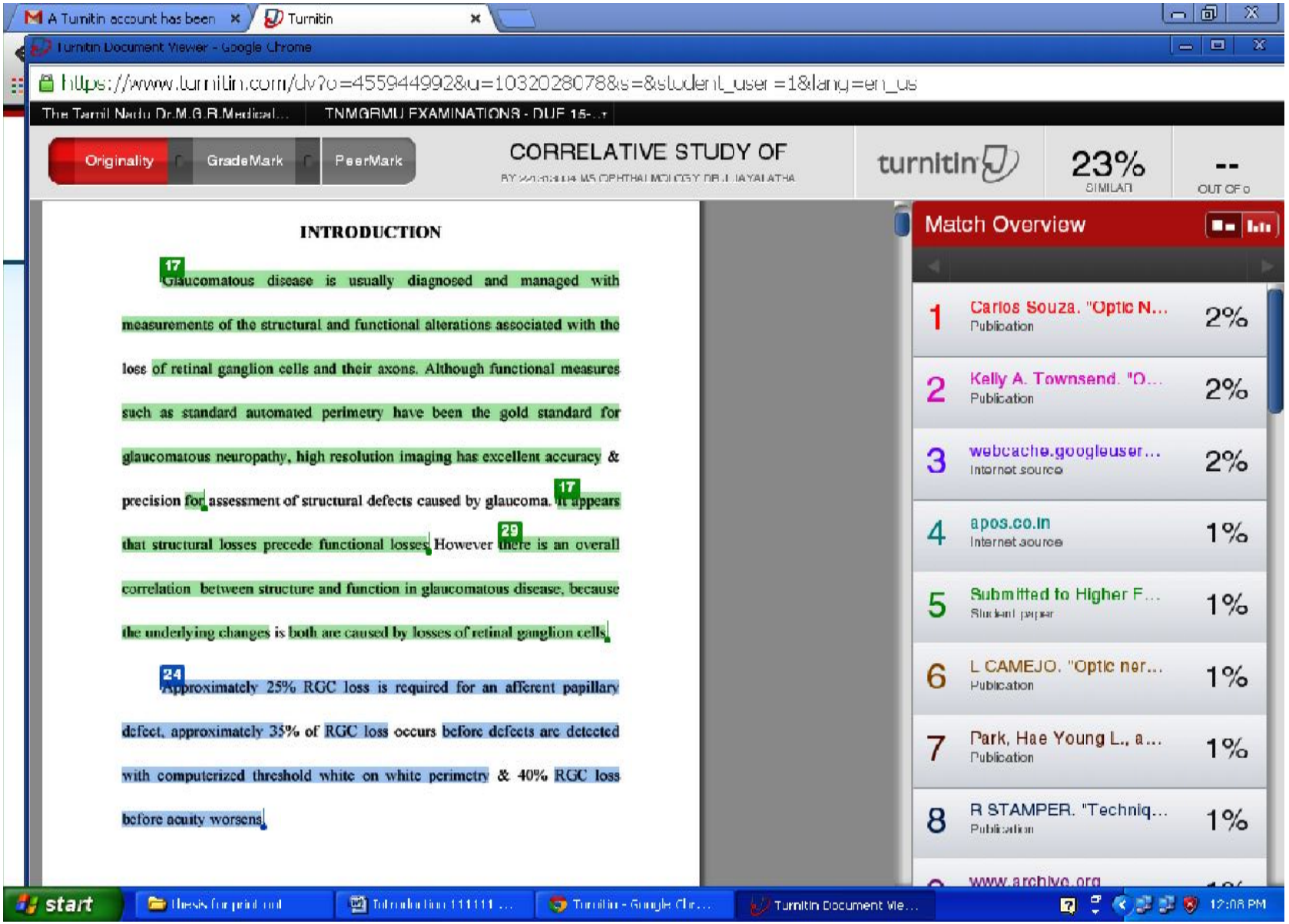
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INTRODUCTION
17 Glaucomatous disease is usually diagnosed and managed with measurements of the structural and functional alterations associated with the loss of retinal ganglion cells and their axons. Although functional measures such as standard automated perimetry have been the gold standard for glaucomatous neuropathy, high resolution imaging has excellent accuracy & precision for assessment of structural defects caused by glaucoma. 17 It appears that structural losses precede functional losses. However 29 there is an overall correlation between structure and function in glaucomatous disease, because the underlying changes is both are caused by losses of retinal ganglion cells.
24 Approximately 25% RGC loss is required for an afferent papillary defect, approximately 35% of RGC loss occurs before defects are detected with computerized threshold white on white perimetry & 40% RGC loss before acuity worsens.
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PART – I

INTRODUCTION

DEFINITION

Glaucoma is a chronic progressive optic neuropathy characterized by optic nerve head changes and visual field changes, the most consistent & reversible factor being use in Intra ocular pressure.

Glaucomatous disease is usually diagnosed and managed with measurements of the structural and functional alterations associated with the loss of retinal ganglion cells and their axons. Although functional measures such as standard automated perimetry have been the gold standard for glaucomatous neuropathy, high resolution imaging has excellent accuracy & precision for assessment of structural defects caused by glaucoma. [8]It appears that structural losses precede functional losses However there is an overall correlation between structure and function in glaucomatous disease, because the underlying changes is both are caused by losses of retinal ganglion cells.

Approximately 25% RGC loss is required for an afferent pupillary defect, approximately 35% of RGC loss occurs before defects are detected with computerized threshold white on white perimetry & 40% RGC loss before acuity worsens.

ANATOMY

GANGLION CELL COMPLEX:

The nerve fiber layer, ganglion cell layer and inner plexiform layer which contains respectively of the axons, cell bodies and dendrites of the ganglion cells are collectively called as ganglion cell complex. (Figure:1)

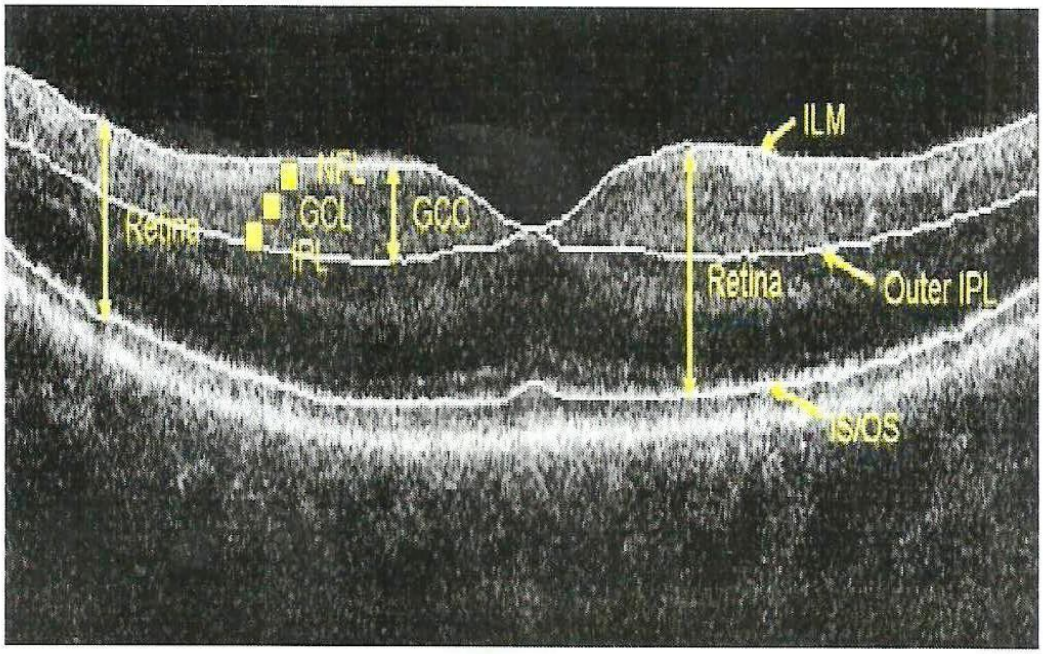


Fig:1 Ganglion Cell Complex

GANGLION CELLS

Finally the ganglion cells are responsible for transmitting visual information from the retina to the brain.

The ganglion Perikarya are located in the ganglion cell layer, while their dendrites make contact with bipolar and amacrine cells in the Inner Plexiform layer.

Upto 20 different ganglion cell types have been described in the human retina.

TWO MAJOR TYPES ARE

1) **MIDGET GANGLION CELL** (also known as Por β cell)

It is a small cell with a relatively small dendritic arbor. It receives input from midget bipolar cell at a ratio of upto one-one in the fovea.

2) **PAROSOL GANGLION CELL (Mor α cell)**

It has a much more extensive dendritic arbor that resembles an opened umbrella in histological preparations of the retina.

RETINOPTIC PROJECTION

	M (magno cellular Pathway)	P (Parvo cellular Pathway)	K (Konio Cellular Pathway)
Approximate Number of retinal cells	10 -11%	80%	9-10%
Receives input from	Parasol retinal ganglion cells	Midget retinal ganglion cells	Mainly bistratified ganglion cells
Projection in LGB	Magnocellular pathway (most ventral layers 1-2)	Parvo cellular pathway (most dorsal layers 3-6)	Within and between principal layers (interlaminar)
Sensitive to motion	Low contrast high temporal frequency (ie motion stimulus)	Color, high contrast and low temporal frequency (ie static stimulus)	Short wave length (blue yellow perimetry)

MECHANISM OF AXONAL TRANSPORT IN GANGLION CELLS:

Because of the anatomic distance between the retina and the brain, the ganglion axons require effective mechanisms for transport of metabolites and

organelles away from (anterograde) and back to (retrograde) the ganglion cell nucleus.

Axonal transport occurs at slow (<10 mm / day), high (hundreds 0f mm / day) or intermediate velocities. Most transport is slow and anterograde.

Axon transport is an active process that requires ATP which is supplied by the mitochondria in the axon. Interference with anterograde transport at the lamina cribrosa results in pathologic disc swelling.

The ganglion cell action potentials are similar to digital or frequency modulation, while the slow graded potentials of the rest of retina are analogous to amplitude modulation.

The ganglion cells which produce propagated spikes are of two types in terms of their centre response. “on - centre” cells that increase their discharge & “off- center” cells that decrease their discharge upon illumination of the Centre of their receptive fields.

GANGLION CELL LAYER:

This layer contains about 1.2 million ganglion cells as well as a number of other cell types including “displaced” amacrine cells, astrocytes, endothelial cells & pericytes.

The thickness of the ganglion cell layer is greatest in the perifoveal macula consisting of between 8 & 10 row of nuclei (60-80 mm), decreases to a single row outside the macula (10-20) & is absent from the foveola

NERVE FIBER LAYER:

Ganglionic axons travel towards the optic Nerve head within the nerve fiber layer. Thin and difficult to discern in the far periphery, the nerve fiber layer becomes thicker towards the disc as a result of the convergence of all retinal ganglion axon fibers on the optic disc.

ARRANGEMENT OF NERVE FIBER LAYER:

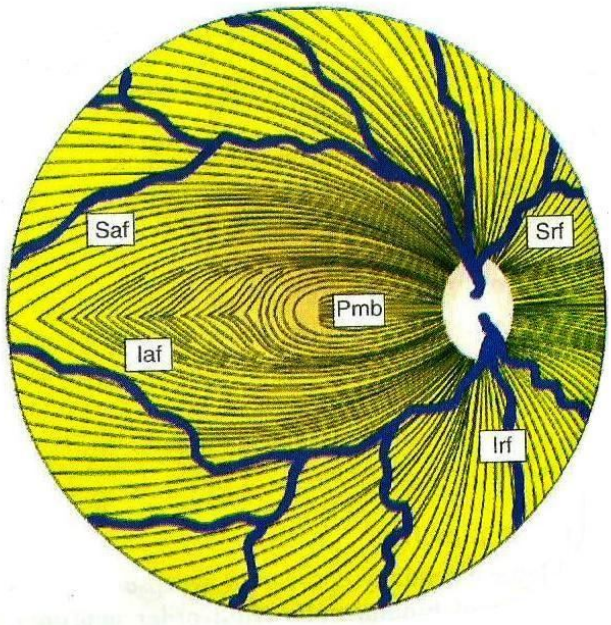


Fig: 2 Arrangement of Retinal nerve fibers

Temporal to the disc lies the macula which has the highest density of ganglion cells. Axons from the macula project straight to the disc forming the papillomacular bundle. (Figure:2)

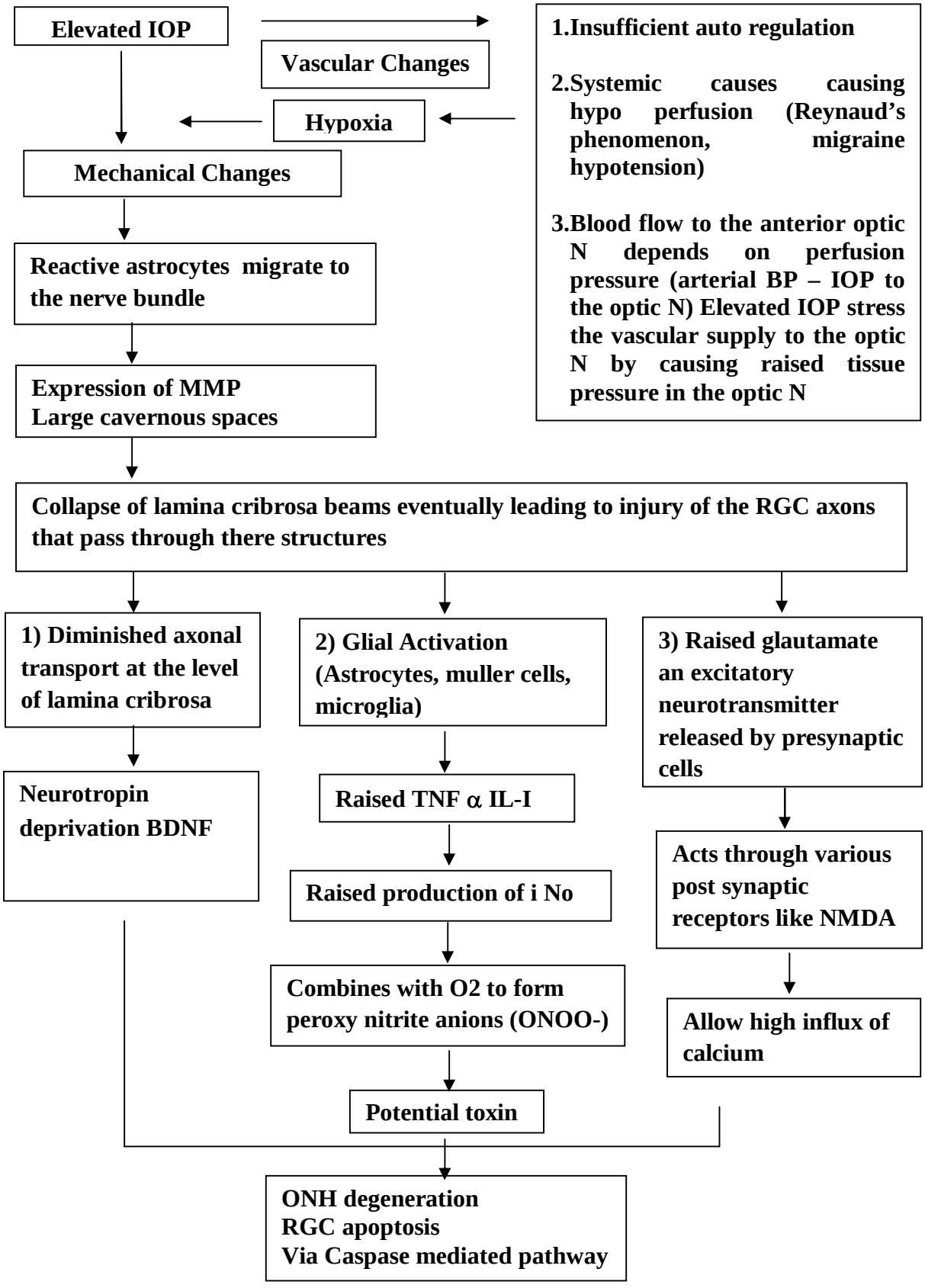
The [4]superior and inferior nerve fibers are much thicker (almost 200 mm) compared to the papillomacular bundle (65mm) and is easier to seen on clinical examination especially in the red – free light.

Nasally axons enter the nasal half of the optic disc more or less straight.

In addition ganglion axon fibers do not cross the horizontal meridian.

PROPOSED MECHANISM OF GANGLION CELL DEATH IN GLAUCOMA :

[7]The neurodegeneration seen in glaucoma is due to end result of apoptosis (Programmed cell death) of the Retinal ganglion cells & it occurs without eliciting an inflammatory response


Elevated IOP
Vascular Changes
Hypoxia
Mechanical Changes
Reactive astrocytes migrate to the nerve bundle
Expression of MMP
Large cavernous spaces
1.Insufficient auto regulation
2.Systemic causes causing hypo perfusion (Reynaud's phenomenon, migraine hypotension)
3.Blood flow to the anterior optic N depends on perfusion pressure (arterial BP – IOP to the optic N) Elevated IOP stress the vascular supply to the optic N by causing raised tissue pressure in the optic N
Collapse of lamina cribrosa beams eventually leading to injury of the RGC axons that pass through there structures
1) Diminished axonal transport at the level of lamina cribrosa
2) Glial Activation (Astrocytes, muller cells, microglia)
3) Raised glautamate an excitatory neurotransmitter released by presynaptic cells
Neurotropin deprivation BDNF
Raised TNF α IL-I
Raised production of i No
Acts through various post synaptic receptors like NMDA
Combines with O2 to form peroxy nitrite anions (ONOO-)
Allow high influx of calcium
Potential toxin
ONH degeneration
RGC apoptosis
Via Caspase mediated pathway

FIELD CHANGES CORRESPONDING TO NERVE FIBER LAYER DEFECT:[3]

1) ISOPTER CONTRACTION

Peripheral isopter contraction may be significantly smaller prior to any field loss.

2) BARING OF THE BLIND SPOT / ENLARGEMENT:

Exclusion of the blind spot is also considered to be early field defect in glaucoma.

3) ANGIO- SCOTOMATA:

They are long branching scotomata above or below the blind spot, which are presumed to be resulted from shadows created by large retinal vessels and are felt to be an early change of glaucoma.

4) ISOLATED PARACENTRAL SCOTOMATA :

It is an island of relative or absolute visual loss within 10^{o} of fixation. (Figure:3)

5) SEIDEL'S SCOTOMA:

If the blind spot enlarge in an arcuate manner, it is called seidel's scotoma & may be seen in early glaucoma.

6) BJERRUMS OR ARCUATE SCOTOMA:

An arcuate scotoma occurs in the area 10-20^{o} from fixation. In its full form,an arcuate scotoma arches from the blind spot and ends at the nasal raphe, becoming wider & closer to fixation on the nasal side. (Figure:4)

7) ROENNE'S NASAL STEP:

A nasal step is a relative depression of one horizontal hemifield compared with the other. (Figure:5)

8) TUBULAR FIELD

Along with double arcuate scotoma leads to tubular field of vision (tubular vision) in which only central vision remains clear.

9) TEMPORAL ISLAND OF VISION

Lastly only a Paracentral temporal island of vision persists, central vision being abolished

10) Ultimately all the nerve fibers are destroyed with no perception of light.

GLAUCOMA SUSPECT:

DEFINITION:

[6]A glaucoma suspect is defined as an adult who has open angles and one of the following findings in atleast one eye.

1) An optic nerve or nerve fiber layer defect suggestive of glaucoma.
2) A visual field abnormality consistent with glaucoma.
3) An elevated IOP greater than 21mm Hg.

HIGH RISK GLAUCOMA SUSPECT:[5]

High risk glaucoma suspect include patients who have one or more of the following.

1) IOP consistently > 30mm HG.
2) Thin central corneal thickness.
3) Vertical cup-to-disc ratio>0.7
4) Older age
5) Abnormal visual field. Eg: Increased pattern standard deviation on Humphrey visual field test.
6) Presence of exfoliation or pigment dispersion syndrome
7) Disc haemorrhage.

8) Family history of glaucoma or known genetic predisposition.
9) Fellow Eye of patient with severe unilateral glaucoma (Excluding secondary glaucoma)
10) Ocular risk Factor
    a) Suspicious disc appearance
    b) Myopic
    c) Low optic nerve perfusion pressure ,
    d) Steroid responders
11) Systemic Risk Factors
    a) Sleep apnoea
    b) Diabetes mellitus
    c) Hypertension
    d) Cardiovascular Disease
    e) Hypothyroidism
    f) Migraine

DOCUMENTATION

1. IOP

2. CCT

3. Optic Nerve head C:D ratio

4. NFL

5. Visual fields

WHEN TO TREAT

1. high risk-suggest treatment

2 .moderate risk-can initiate treatment if appropriate or monitor closely

3.Low risk- monitor IOP as well as optic nerve structure and function - treat if evidence of progression.

PRIMARY OPEN ANGLE GLAUCOMA:

DEFINITION:

It is a chronic progressive Optic neuropathy characterised by open angles, visual field changes and optic nerve head changes, the most consistent and reversible risk factor being rise in Intra ocular pressure.

TRIAD IN PRIMARY OPEN ANGLE GLAUCOMA:

1) Raised Intra ocular pressure
2) Optic Nerve Head Changes
3) Visual field Changes.

VISUAL FIELD[3]

Harry moss traquair (1875-1954) defined the visual field as the island of vision surrounded by the sea of darkness.

The island of vision is usually described as a three dimensional graphic representation of differential light sensitivity at different position in space. (Figure:6)

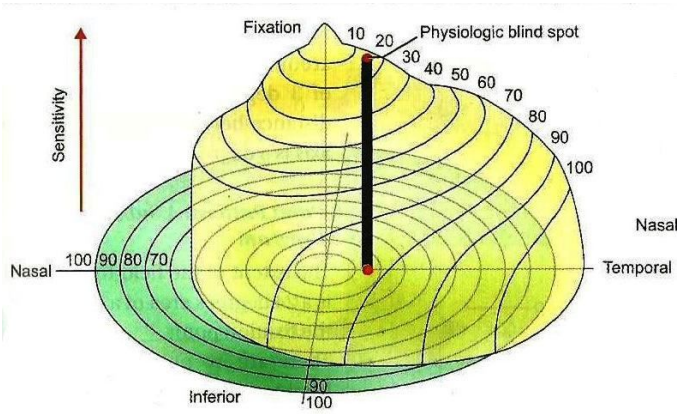


Fig: 6 Hill of Vision

EXTENT OF THE VISUAL FIELD

The boundary of normal visual field measured in degrees from the point of fixation extend on an average to 60 degrees superiorly, 70 degrees inferiorly, 60 degrees nasally & 100 degrees temporally.

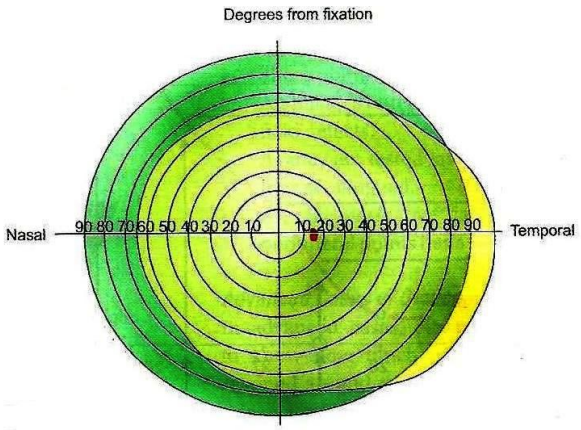


Fig: 7 Extent of Visual Field

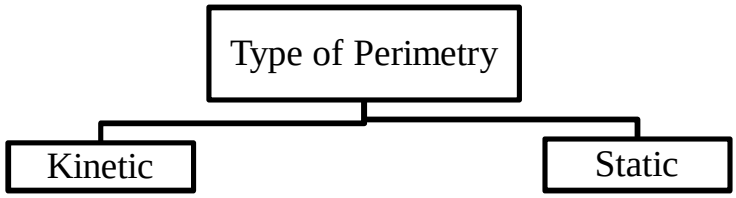
PERIMETRY

If refer to the clinical assessment of the visual field.

Perimetry has traditionally served 2 major purposes in the management of glaucoma

1. Identification of abnormal fields
2. Quantitative assessment of normal or abnormal fields to guide follow upcare.

TYPE OF PERIMETRY



-Confrontation technique

-Bjerrums screen

-Goldmanns perimetry

Humphrey

Octopus

KINETIC PERIMETRY:

Role of semiautomatic – computer assisted kinetic perimetry

1. For examining peripheral field in neuro ophthal
2. In end stage glaucoma
3. In patients who have difficulty collaborating with an automatic test

AUTOMATED PERIMETRY – A HISTORICAL EXCURSION

In 1972, Frankheuser et al, developed the principles and concepts of automated perimetry and established the standards of present day automated perimetry.

In 1985 Flammer introduced the examination program G_1

At the same time Bebie et al suggested the use of the cumulative defect curve and Gronzalez de la Rosa with his Top Strategy.

In 1980s Octopus 2000 and Octopus 500 were introduced.

The octopus 1-2-3 was the direct projection perimeter which does not require any cupola and was introduced in 1980

In 1990's octopus 101 was introduced and was the first perimeter in windows and can be upgraded to SWAP.

Octopus 300 is similar to 101 but have added software.

AUTOMATED PERIMETRY – INTRODUCTION

THE NORMAL VISUAL FIELD

If would be very difficult to interpret individual visual results without having a reference at hand representing the visual field of a "Normal" observer of the corresponding age group.

The Normal visual field is derived from a large number of examinations obtained in multicentric studies. This data is stored in the software and can be displayed together with the individual results.

VARIABLES IN VISUAL FIELD TESTING[3]

PATIENT ARTIFACTS

1. **AGE**

With age, the visual field has a linear decrease in sensitivity and the slope steepens. Mean sensitivity of visual field decreases approximately 0.58 to 1.00 dB per decade.

2. **FIXATION:**

Results vary with the quality of fixation control.

3. RELIABILITY

Misunderstanding the test, fatigue, inattentiveness, systemic illness can all affect the Patient's reliability.

EYE ARTIFACTS

1. PUPIL SIZE

<3mm can cause generalized depression of the visual field.

2. REFRACTION

Should have distance prescription with proper addition for near vision.

3. MEDIA OPACITY

Any opacity of the ocular media can cause localized or generalized depression of visual field.

EXAMINATION ARTIFACTS

1. Equipment results vary with different equipment.
2. Test results vary with different types of tests.
3. Software results vary with different testing or interpretation algorithms.

ANALYSIS ARTIFACTS

1. Is the visual field normal? Requires standards for normal.
2. Has the visual field changed? Requires knowledge of fluctuation.
3. Misinterpretation.

OCTOPUS PERIMETER 301

If is a direct projection perimeter for examinations of the central visual field 30^{o}. (Figure : 8)

PARTS:

OPTICAL UNIT

It is a direct projection system which projects the stimuli directly into the patient's eye via the optical unit which replaces the cupola.

So it does not require dark room for examinations.

HEADREST

Forehead rest consists of sensor which provides information about the correct head position.

TRIAL LENS HOLDER

The stimulus seems coming from infinity and thus only distance correction is required.

HOUSING

The Optical unit & the electronics are protected by housing with three sections.

OPERATING UNIT

Data entry can be made by via the touch screen & information is made available via LCD monitor.

PATIENT RESPONSE BUTTON

It is connected on the underside of forehead rest.

EXTERNAL CONNECTIONS

Connections for PC & Printer are provided on the connector panel.

LIGHT SOURCES

There is built in LED's for background illumination, fixation targets & stimulus. It does not produce active heat and no active coiling is required.

LIGHT INTENSITIES

The background and stimulus intensity are measured with independent photo sensors & are calibrated to their present reference values every time, the perimeter is switched on.

STIMULUS

The duration & brightness of stimuli are controlled electronically

FIXATION MONITORING

Gaze monitoring is done by projecting Infra red light on to the cornea & checking for the corneal reflex relative to the pupillary center, recorded using a camera & displayed on the LCD monitor.

PRE-SETTING EXAMINATION

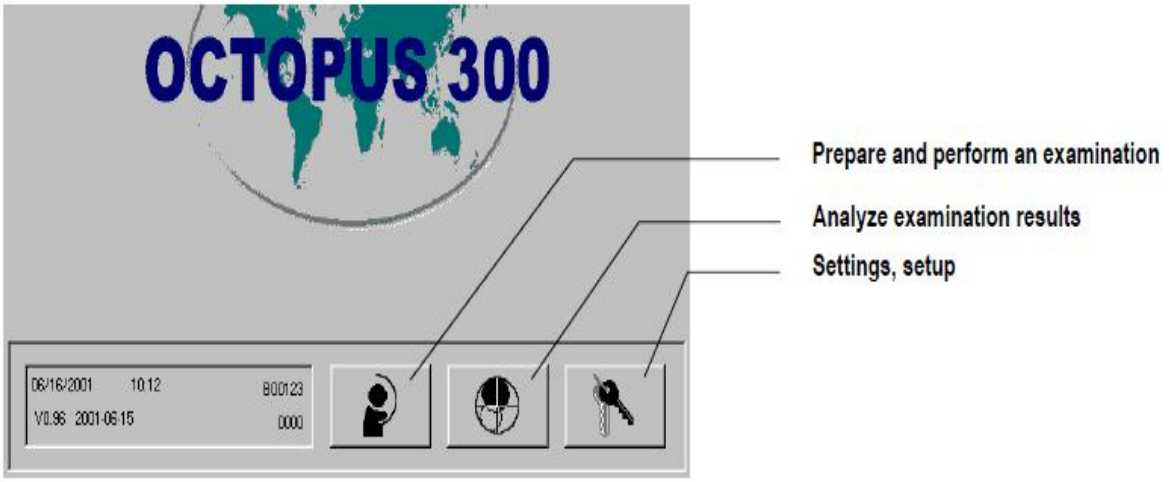


Fig: 9 Pre- Setting Examination

PROGRAM VARIANTS (Figure : 10)

PROGRAMS AVAILABLE

G_1, 32, M_2 ST, LVC

STRATEGY AVAILABLE:

NORMAL ,DYNAMIC,TOP

STAGES /AUTO

Specify the number of examination stages which should be gone through.

CATCH TRIALS

See the number of catch trials as a percentage (%) which should be presented during the examination. same number for positive & negative catch trials.

SELECTING THE PERIMETER METHOD:

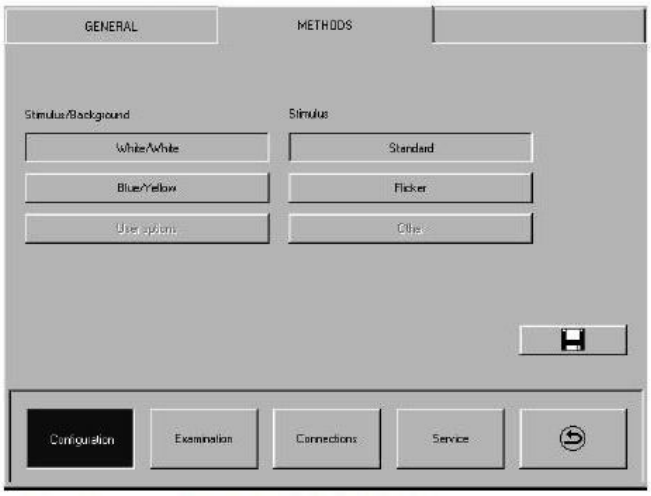
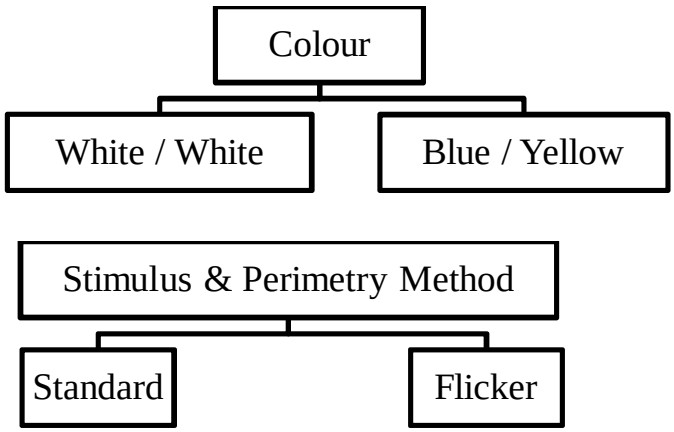


Fig: 11 Selecting the Perimetry Method

a) Stimulus & Background

b)



DEFINING USER – DEFINED TESTS (Figure: 12)

Test locations	Specify the number of test locations which are to be examined. The number in front of the slash (/) defines the number for a square test area, the number after the slash (/) the number for a round one
Pattern	Distribution of the test locations linearly or non-linearly over the test area.
Shape	Square or round test area
Fixation target	Set the fixation target to be displayed for the patient during the examination. Test locations which collide with the fixation target, are eliminated from the program.
Strategy (TOP not available)	Specify the examination strategy which controls the examination process.
# Phases	Define the number of phases which are to be gone through
Stimulus size	Set the stimulus size according to Goldmann III or V.
Stimulus duration	Set the duration of the individual stimuli.

MEASURMENT STRATEGIES

NORMAL TESTING STRATEGY

The visual field determination starts at all test points from the expected age corrected minus 4 decibels. A ‘no’ answer drops the stimulus luminance by 6 dB if the first response to a minus 4 dB start is negative. A brighter light stimulus is projected which is 8 dB less to quickly approach the depressed sensitivity of the test point. Once the anchor points are determined further testing in a 4-2-1 dB step approach at each of the predetermined test points are determined from the data obtained from the estimated hill of vision rather than starting from normal hill of vision values which would make the testing tedious. This is approximately five questions per test point hence sensitive enough to detect shallow pathology. Normal strategy takes about 15 to 18 minutes per eye to complete a visual field examination.

DYNAMIC TEST STRATEGY

The Stimulus luminance step size (bracketing) adapts to the slope of the FOSC. When the depth of the defect is deep, the step size increases from increment steps of 2 dB to 10dB to achieve final calculated value from the last

two tested values. The accuracy obtained with this test is comparable to the regular full threshold test with 4-2-1 dB strategy.

The test duration is about 40 to 50 percent in severely depressed fields and 30 to 40 percent in marginally depressed fields when compared to normal threshold. Short- term fluctuation values may also be calculated by retesting all locations in the second phase if additional information is needed.

TENDENCY ORIENTED PERIMETRY

TOP divides the test location in the visual field into evenly intermingling grids. The four grids are examined one after another and the locations of the other three matrices are adjusted to get new values by interpolation. The examination starts at half the value of the expected age corrected value, which in dB is 8/16 of the expected normal value. Then the testing begins with steps in relation to the patients age corrected value, i.e. 4/16, 3/16, 2/16 and finally 1/16. These steps may be in either direction to determine the final threshold of dB sensitivity. Gray scales show a rounded effect in TOP compared to regular threshold gray scale values because of the adjustments of the neighboring points. Hence, the average sensitivity values obtained may be little ‘shallow’ compared with regular threshold testing.

OCTOPUS EXAMINATION PROGRAMS

PROGRAM G1/G2

The two programs are identical in the central 30^{o} consisting of 59 test point locations and differ only in the peripheral 15 additional points tested between the 30^{o} and 60^{o} in G2. The G2 is a program optimized for Octopus 101/900 series perimeter. The G1 program test locations respect the topography of the nerve fiber layer and are weighted to detect the nasal step in glaucoma. The foveal and paracentral areas have resolution of 2.8^{o} in the G1/G2 programs compared to 4.2^{o} resolution in a classical program 32 test location. The increased resolution in the foveal area gives a good follow-up when there is a fixation threat, without the need of an additional visual field test for the fovea.

All strategies can run on the G1 and G2 program. The phase 3 (screening the periphery) and phase 4 (quantifying the periphery) runs in the 101 and 900 series. These perimeters are used in research and teaching settings.

PROGRAM 32

There are 76 test locations in a grid pattern with a resolution of 6^{o}.This program is not related to the topography of the nerve fiber layer or pathology,

with both eyes having identical pattern of test locations. The program 32 is still an option if old follow up was done with this program.

It may also be used in neurological cases where this program defines the vertical and horizontal meridians well. Phase 2 testing may be done to assess the short term fluctuation in normal and dynamic strategy.

PROGRAM M2

The macular program was designed for detection and follow up of central and paracentral visual field defects in patients with neurological diseases,macular or perimacular diseases.

The M2 program has 45 test locations which are tested in two stages consisting of the central 4^o and the area between 4^o and 9^o.The 45 test locations in the central 4^o gives a 0.7^o resolution with a Goldmann size III .

The additional 36 test locations situated in the outer 4^o and 9^o gives this program the highest resolution in the central 10^o of the visual field.

The M2 program can be run using the TOP, dynamic or normal strategy to define the visual field pathology in question.

THE N1 NEUROLOGIC PROGRAM

It is a multistep examination program which takes into account the possible displacement of blind spot due to extraocular muscle and avoids artifacts due to hemianopia or hemineglect.

PROGRAM ST

It is a glaucoma screening test. The test locations are the same as G1 except that the only qualitative data is obtained in 3 to 4 minutes.

OCTOPUS STAGING OF VISUAL FIELD

Normal strategy typically takes 18 to 20 minutes to complete the tests. The single pass visual field test was modified into staged modules and tests points so that the first tested points give the best results without the influence of fatigue. Each of the four stages behaving as independent test with result outcome accumulated thus far. The results obtained in the first two stages account for almost 80% of the result.

TEST PHASES IN OCTOPUS PERIMETER

After one or two stages of visual field testing in the first phase, one of four options exist in second phase of visual field testing.

1. The test may be saved, printed or stopped.

2. The test points may be retested to ascertain the short term fluctuations.

3. Quantify relative defects.

4. When data already indicates the deviation from normal then additional peripheral test points may be tested to confirm clinical findings

PRINT OUT (Figure: 15)

PATIENT DATA-① (Figure: 13 & 14)

Name, identity number, date of birth, age, sex, best corrected visual acuity, refractive correction, IOP & pupillary diameter.

EXAMINATION DATA-②

Consists of the programme chosen, strategy used stages & phases conducted, target size used, stimulus duration & background illumination. The catch trials also depicted.

GRAY SCALE -⑤

It depicts the sensitivity in different shades where the darker colors depict deeper defects.

VALUE TABLE -③

It displays the actual retinal sensitivities measured in decibels at all the tested locations.

COMPARISON TABLE 4 and 8

If compares the retinal sensitivity to the age matched normal value for each point. It the test value is within 4 dB of normal a plus (+) symbol is printed. If the mean threshold is 5 or more dB different from the normal value, the actual difference between the two is printed. In the resulting comparison table higher number on the printout represent deeper depressions.

If the patient fails to respond to the brightest stimulus, the machine prints a black square symbol indicating absolute defect.

The comparison table is also depicted in a probability plot showing the probability of defect in general population.

CORRECTED COMPARISON TABLE -⑦

It is derived by subtracting the deviation from the Bebies curve from the defect values to show any hidden localized defects after correcting for any generalized depression of the hill of vision.

BEBIE'S CURVE -⑥

Bebies curve is a graphic representation to aid in the quick assessment of the characteristics and depth of the defects.

The curve has a band showing the range of normal's which corresponds from the 5^{th} to 95^{th} percentile.

Any curve falling outside the band is considered abnormal.

A pure generalized depression will yield a curve which is same in shape but is lower than the normal.

In the presence of focal loss, the right aim of the curve will steepen in the curve.

VISUAL FIELD INDICES -⑨

1) MEAN SENSITIVITY

It represents the arithmetic mean of the threshold determined at all of the points in the field. It is represented in dB. Mean Sensitivity alone is not very valuable.

2) MEAN DEFECT

The arithmetic mean of the difference between the values measured in

Examination and that of the age matched normal's.

It is a measure of generalized depression rather than a focal change. It is represented in dB

In Octopus +ve - depression
-ve - normal.

Humphrey -ve - defect.

LOSS VARIANCE

It represents the focal non uniformity of the visual field loss.

It reflects focal alterations rather than an overall depression of the field.

In cases where the defect is uniformly distributed throughout the field the LV is small. Whereas in cases of localized defects the LV is high.

The LV is influenced by localized field loss, increased SF and measurement error.

SHORT – TERM FLUCTUATIONS

It is obtained by testing the threshold twice at the same locations & is used to determine the corrected loss variance. SF represents the intra test variability. SF value of less than 1.4 dB is considered not significant,

1.5 - 2.5 dB - Moderate intra test variability

> 2.5 dB – significant.

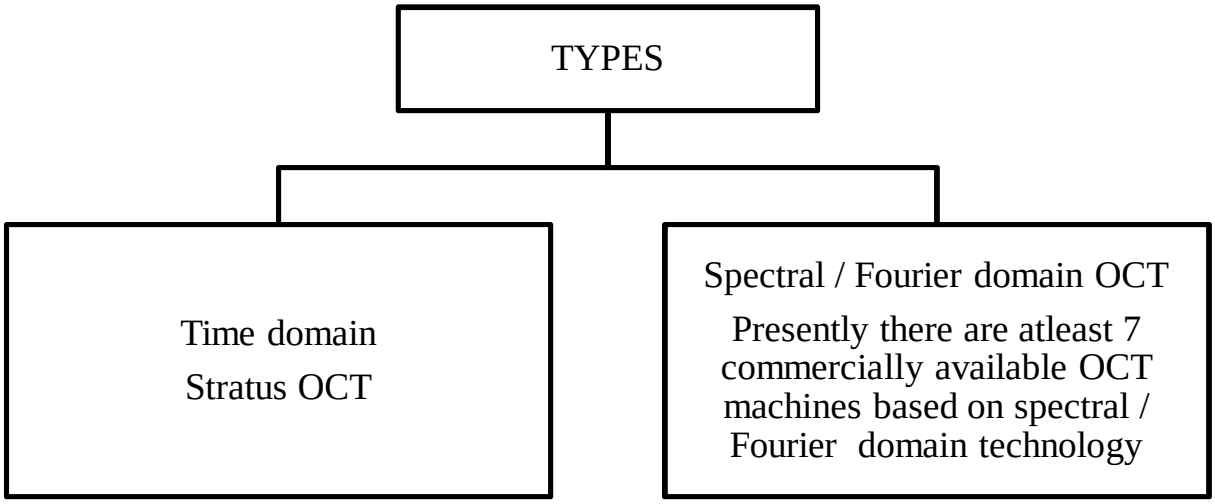
CORRECTED LOSS VARIANCE

It represents the non uniformity of the field independent of the short term fluctuations. CLV is derived by subtracting the SF factor from the LV to get a more sensitive value for detection of early localised defects.

OPTICAL COHERENCE TOMOGRAPHY[2]

It is a non invasive non contact imaging system which provides high resolution cross sectional images of the optic nerve head, macula, RNFL of less than. 10μm axial resolution using light waves.

TYPES (Figure: 16)



PRINCIPLE OF SD OCT (Figure: 17 & 18)

It is a diagnostic imaging technology that utilizes michelson's interferometry and low coherence light in near infra-red range.

A broadband width near-infrared light beam (840 nm) is projected. The beam is split to the tissue of interest (say retina) called as probe beam & to a reference mirror at a fixed position (reference beam). A positive interference is produced when light reflected from the retina & reference mirror arrives Simultaneously.

A spectrometer is utilized in the detector aim of the interferometer uses a grating or a prism to spread the light into a spectrum.

The spectrum is typically detected by a line camera.

The instrument uses fourier analysis to analyses the images according to the light wavelength record.

The immediate advantage of this technology is high number of scans acquired per second approximately 27000 A-scans per second making 3D imaging possible & practical in a clinical environment.

ADVANTAGE OF SPECTRAL DOMAIN OCT OVER TIME DOMAIN OCT

		SD OCT	TD OCT	Benefits of SD OCT
1	Light Service	840 nm Broader band width	820 nm	Provides higher resolution.
2	Detector	Spectrometer	Single detector	No moving parts faster scan acquisition
3	Axial resolution	6-7 μm	10 μm	Better visualization of retinal layers and pathology
	Transverse resolution	10μm	20μm	
4	Maximum A Scans per B scans	8000	512	Better visualization of tissue pathology
5	Scan depth	2mm	2 mm	Slightly better penetration of light
6	Scanning speed	About 20,000 A scans per second	400 A – Scan per second	Better registration 3D scanning & analysis
7	Scan protocol	Raster scan	Line scan limited amount of data interpolation	Large number of data points more precise segmentation of retinal layers.
8	Scan registration	Scan registration done	No scan registration – operator has to centre the scan circle during each visit. decentration effects - common	Better repeatability reproducibility & reliability

THE OCT MACHINE –A HISTORICAL REVIEW

The use of optical coherence in biological systems was first described by Huang et al in 1991.

Optical coherence tomography was first demonstrated in 1991 by a Massachusetts Institute of Technology by Fujimoto and his group.

First in-vivo studies of the human retina done with OCT in 1993.

First commercial use of OCT in ophthalmology started in 1997 and becomes standard care for retinal imaging.

Humphrey's system released its first unit in 1996 and gained federal drug administration clearance in 2002.

OCT 2000 (OCT 2) introduced in the year 2000 and stratus OCT (OCT 3) which became commercially available in 2002 .

The first SD- OCT in vivo scans presented were by Wojtkowski and colleagues in 2001.

SD-OCT –the first high speed, high resolution OCTs became commercially available since 2006.It uses fourier analysis, resulting in faster scan acquisition times, resulting in a large increase in the amount of data that can be obtained during a given scan duration making it possible to construct a 3D image.

THE OCT SYSTEM COMPRISES (Figure: 19)

Fundus viewing unit

Interferometric unit

Computer display

Control panel

Colour inkjet printer

PROCEDURE

INITIAL PREPARATION

1) Data entry made for a new patient
2) A 3mm pupil is necessary for adequate visualization.
3) Patient is seated with his chin on the chin rest and eye at the level of the mark on the side of the frame.
4) Then the Z-offset of the image is optimized to bring the image to the centre. The polarization is optimized next to Create a clear image.
5) A signal strength of 5 and above gives a clear image.

FIXATION

Patient is asked to look inside the ocular lens-Internal fixation-onto the green target light inside the red rectangular field or external fixation-onto the

external target by the other eye in patient with poor vision. The patient is encouraged to blink in between scan acquisition.

GLAUCOMA PROTOCOLS

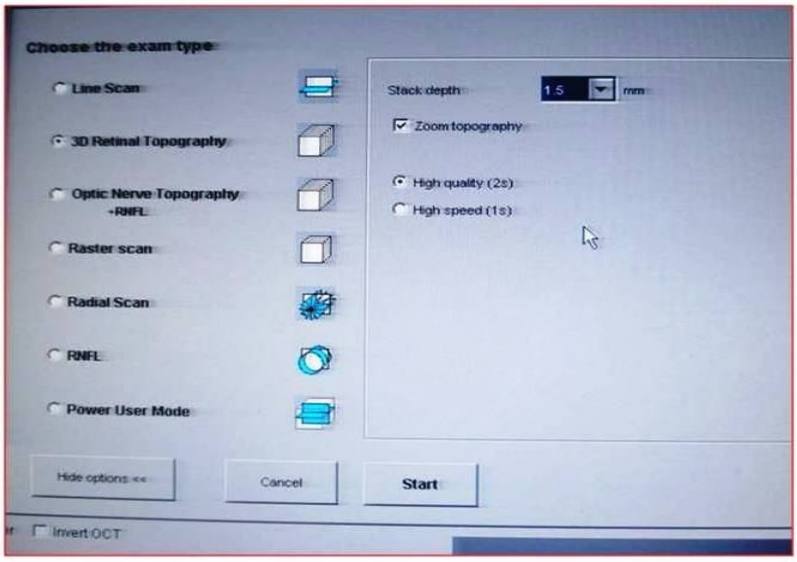


Fig: 20 Glaucoma Protocol

RNFL -3.4 mm Circular scan

ONH topography - Optic Nerve topography - RNFL

- Based on Retinal Thickness Measurements from 200 C-scans centered on optic disc.

Macula - 3D Retinal topography which acquires 200 C- scan OCT cuts in 2 seconds

SCAN ACQUISITION

Once the protocol is selected, Scan acquisition window is activated. Scan image is seen left of the screen & video image is seen on the Right side of the screen.

LINE SCAN

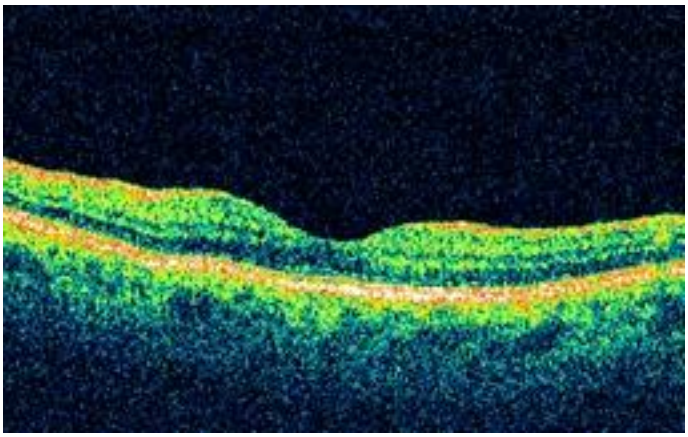


Fig: 21 Line Scan

1) Fovea – area of thinning
2) RPE, RNFL & Choriocapillaries are highly reflective and appears red / white
3) Photoreceptor, Choroid & pockets of fluid are low reflective layers and appears blue / black

SCAN PLACEMENT

The scanner activates by default in the scan alignment mode is which the scanner traces a aiming pattern which is seen on the video monitor. This is useful for scan placement on the desired position on the optic disc or retina.

CAPTURE STACK

Once the video image is satisfactory a scan image is placed satisfactorily scan is frozen. If the Quality of the scan image frozen on screen satisfactory, it is saved using save button.

ANALYSIS PROTOCOLS[3]

OCT RNFL THICKNESS AVERAGE ANALYSIS REPORT PRINT OUT

(Figure: 22)

1.Type of report

2.Patient information

3.RNFL thickness graph with color coded normative database

4.clock hour thickness and quadrant thickness

5.Fundus image showing scan placement and single OCT scan

6.signal strength

7.overlay graph of RNFL thickness for both eyes

8.scans included in the analysis

9.measured parameters

10.percentiles for normal distribution.

Circular scan 3.4mm diameter centered on the optic disc. Line scan length of about 10.87μm is obtained by unfolding retina.

It produces a characteristic double lump pattern owing to the raised RNFL thickness at the superior & inferior poles of the disc.

The RNFL curve is drawn as a black line over a back ground of color-coded shaded areas representing RNFL thickness classification according to the normative database. (green means within normal limits, yellow means borderline and red means outside normal limits).

The peripapillary RNFL is divided into 12 clock hours and four quadrants. All are classified in a normative database color-coded manner.

The average thickness is calculated for both eyes and it appears at the bottom of the thickness measurement table. The thickness values are also color coded.

The RNFL serial analysis protocols allow the comparison of RNFL thickness over time. The RNFL thickness graphs of up to 4 visits are super imposed on the same chart & each visit is color coded.

OPTIC NERVE HEAD ANALYSIS REPORT (Figure: 23)

1.Type of report

2.patient and scan information

3.single OCT image

4.single scan analysis parameters

5.signal strength

6.overall analysis parameters

7.Fundus image showing scan placement

8.physician's interpretation

INDIVIDUAL RADIAL SCAN ANALYSIS

They are primarily based on two automated algorithms

(i) A segmentation algorithm that determines the location of the inner limiting membrane. As shown by a blue line at the surface.

(ii) The other algorithm that detects the retinal pigment epithelium (RPE / Bruch's membrane) termination indicated on the printout as blue circles with crosshairs inside.

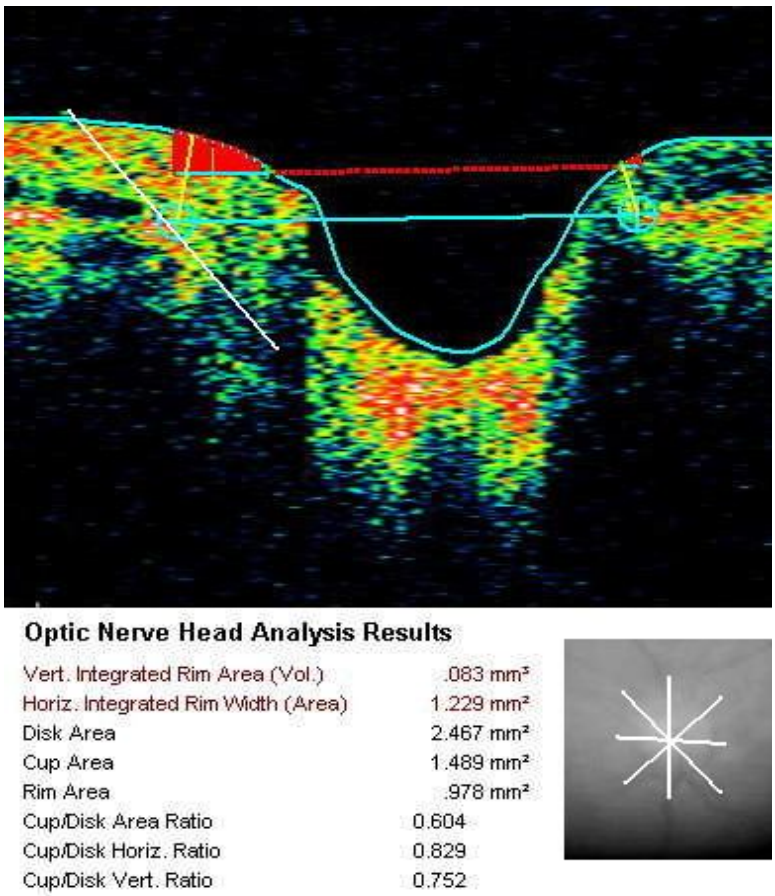


Fig: 24 Optic Nerve Head Analysis

(iii) The OCT defined the disc diameter as the horizontal distance between two points of RPE / Bruch's termination.

(iv) A second line in blue is drawn parallel to disc diameter & offset anteriorly by 150 microns. To define the plane that separates cup from rim. This is shown by red dotted line. The cup diameter is the horizontal distance between the two intersections of the red dotted line with the ILM surface.

iv. Rim length horizontal is calculated as the disc diameter minus cup diameter.

v. The Rim area for the vertical cross section parameter is the total area of the red-shaded section of the scan.This area is bordered by the yellow vertical lines extending up from the RPE termination,the ILM surface and the red dotted line separating cup and rim.

OVERALL "OPTIC NERVE HEAD ANALYSIS REPORT"

1. Optic nerve head topography scan is obtained by measuring retinal Thickness measurement by placing 200 C-scan centered on the optic disc.
2. Disc Area and cup area is calculated as the area within these margin
3. rim area is calculated as the disc area minus cup area.
4. The cup disc area ratio is calculated as simple ratio of these areas.
5. The cup disc horizontal and cup disc vertical ratios are calculated by taking the maximum cup diameter in the horizontal or vertical direction and dividing it by the maximum disc diameter in the horizontal or vertical direction.
6. There is no normative data available for optic nerve head topography.

RETINAL THICKNESS TABULAR OUTPUT REPORT

(Figure: 25)

1.Type of report

2.Patient and scan information

3.Fundus image and single OCT scan

4.Thickness and volume parameters

5.signal strength

6.color coded thicknes map

7.thicknes map with normative data

8.percentiles for normal distribution

9.colour coded thickness scale

10.physician’s interpretation

The macular 3-D topography provides 200 c-scan cuts in two seconds.

It gives a color coded thickness map with background shaded areas representing the normative database. The retinal thickness measurement for nine macular sectors are provided which is also color coded.

RECENT ADVANCES

SHORT-WAVE LENGTH AUTOMATED PERIMETRY

Short-wave length automated perimetry (SWAP) uses a blue stimulus on a yellow background. Sensitivity to blue light (mediated by blue cone photoreceptors) is adversely affected relatively early in glaucoma. SWAP is more sensitive to early glaucomatous defects but has not been widely adopted because cataract decreases sensitivity to blue light (the brunescing lens acts as a yellow filter) and patients frequently dislike the lengthy test. It is available on newer HFA models.

FREQUENCY-DOUBLING CONTRAST TEST

Ganglion (M) cells with relatively large diameter axons comprise 25% of the ganglion cell population. They are particularly susceptible to glaucomatous damage and appear to be preferentially lost in early glaucoma. A loss of a small number of these cells has a considerable effect on visual function. Psychophysical tests have been devised to target visual function provided by these magnocellular pathways in the detection of early glaucoma.

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damage and appear to be preferentially lost in early glaucoma. A loss of a small number of these cells has a considerable effect on visual function. Psychophysical tests have been devised to target visual function provided by these magnocellular pathways in the detection of early glaucoma.

Frequency-doubling illusion is produced when a low spatial frequency sinusoidal grating (less than one cycle per degree) undergoes high temporal frequency counter phase flicker (>15 Hz). The rapid alternation in which the light bars become dark and vice versa produces the illusion of the grating having doubled its frequency.

The perimeter is a tabletop instrument which can be used under normal room lighting and requires no patching, since the viewing canopy automatically covers the eye not being tested. The device requires minimal training and is relatively portable.

Stimuli are presented in 17 or 19 sectors in the central 20° or 30° depending on the program used, screening or full threshold.

Testing time is short with full threshold programs taking about 5 minutes per eye and screening procedures between 45 and 90 seconds per eye. Because of this most patients prefer the FDT test to conventional perimetry.

Results are displayed and printed together with reliability indices, probabilities, mean deviation and pattern standard deviation. FDT has high sensitivity both in screening to differentiate healthy individuals from those with glaucoma and for quantifying glaucomatous damage. The results are minimally affected by refractive error of up to 6 D and not at all by pupil size. The device has an age-adjusted normative database, as well as a statistical analysis package for immediate evaluation of results.

The Humphrey Matrix is a more recently introduced FDT perimeter which allows extended testing of considerably larger areas of field than the basic screening version. It is thus proposed as being at least comparable to the HFA for refined diagnosis and monitoring

CONFOCAL SCANNING LASER OPHTHALMOSCOPE

HRT is a confocal scanning laser ophthalmoscope, with high axial optical resolution that uses a diode laser-670 nm wavelength, to sequentially scan the retinal surface at multiple focal plan.

The confocal scanning laser ophthalmoscope currently in use is its third generation. The new HRT-3 software (Heidelberg) features improvements in image scaling and alignment, a new diagnostic classification system, and an expanded normative database. The new shape based analysis (the Glaucoma

Probability Score) does not require an examiner to draw a contour line around the optic disc, which decreases the inter-operator variability, and it is independent of a reference plane position

The HRT-3 software has a new, larger normative and ethnic-specific database that adjusts to age-related changes in the optic disc and optic disc size, with perhaps a higher accuracy in the analyses provided by the instrument. The new scaling and alignment algorithm improve the ability to measure stereometric parameters such as area and volume based measurements, height variation contour, and RNFL cross-sectional area. There are currently two progression algorithms on the HRT-3 software: trend comparison analysis (TCA) and ‘trend analysis.

The HRT-3 has an advantage over other imaging technologies in that it is compatible with earlier software versions of itself(HRT-2 and HRT-1), and therefore it is possible to analyze HRT-3 images with prior versions .This allows glaucoma progression to be detected over a much longer period of time, which is a real advantage in longitudinal studies .

DISPLAY

Images of the disc and peripapillary retina are shown at the top of the display.

In the topographic image (top left) the cup is represented in red, neuroretinal rim in green and the connecting slope in blue.

The reflectivity false colour image (top right) is divided into six sectors. Both the neuroretinal rim (green and blue on the topographic image) and the disc area (green, blue and red) are assessed using Moorfields regression analysis, taking into account age and overall disc size. A green tick within a sector indicates it is within normal limits, a yellow exclamation mark borderline and a red cross outside normal limits.

The two cross-sectional images show the amount of cupping in the vertical and horizontal planes. Two lines represent the edge of the optic disc and the single red line represents the arbitrary reference plane.

The mean height contour graph displays the variation of the retinal surface height along the contour line (green). The reference line (red) below this shows the position of the reference plane, designated as the plane of separation between the cup below and the neuroretinal rim above. This reference plane is parallel to the peripapillary retinal surface and is located 50 µm below the retinal surface at the location of the papillomacular bundle on the contour line. It is thus approximately located at the lower extent of the RNFL.

The display of the retinal surface height variation along the contour line begins temporally at 0° (approximate centre of the papillomacular bundle). The height profile is plotted in a clockwise direction for a right eye and a counter-clockwise direction for a left eye. The graph largely corresponds to the course of the RNFL thickness along the disc margin.

The Moorfields regression analysis is depicted as seven colour bar graphs, one bar for each segment and one global bar (bottom right). If the top of the green bar lies above the 95.0% prediction interval then the corresponding disc segment is classified as within normal limits, if it lies between the 95.0% and 99.9% it is borderline, and if it lies below 99.9% it is outside normal limits.

Detailed stereometric data are presented in a table. Readings outside normal are indicated with an asterisk.

SCANNING LASER POLARIMETRY

The GDx (Glaucoma Diagnosis) RNFL analyzer assesses the nerve fibre layer thickness by using its assumed ‘birefringent’ (resolving or splitting a light wave into two unequally reflected or transmitted waves) nature to change the polarization of incident polarized diode laser light; the amount of alteration is directly related to the thickness of the layer. The degree of polarization is assessed over an area of 1.75 disc diameters concentric to the disc and the

profile of the density of the RNFL established; the thicker the RNFL the greater the polarization. The newer GDxVCC (Variable Corneal Compensation) version has eliminated many of the problems of the previous model which hindered its ready clinical acceptance.

Indications are similar to those of the SLO, although there is no macular facility.

Display provides colour images of the optic nerve head and RNFL maps in the four quadrants

The fundus image of the left and right eyes at the top is useful in identifying image quality.

The thickness maps are presented in a colour-coded spectrum from blue to red. Red followed by yellow indicates a thick RNFL whereas blue followed by green shades are consistent with thin RNFL. The map has an hourglass appearance because the RNFL is thickest superiorly and inferiorly.

The deviation maps show the location and magnitude of RNFL defects as tiny colour coded squares (pixels).

The TSNIT (temporal-superior-nasal-inferior- temporal) graph is displayed at the bottom. It shows the actual values for that eye along with a shaded area that

represents the 95% normal range for that age. The curve in a healthy eye should fall within the shaded area and has a double hump pattern because the superior and inferior fibres are thickest. The central printout shows the values for both eyes together.

Parameters for each eye are displayed in a table . The nerve fibre indicator (NFI) at the bottom of the table indicates a global value based on the entire thickness map and is the optimal parameter for discriminating normal from glaucoma. Normal is 1–30, borderline is 31–50 and abnormal is 51–100.

REVIEW OF LITERATURE

According to Dilraj.S.Grewal et al,OCT may be useful for detection of structural progression and in quantifying the velocity of progressive RNFL loss.

According to this study, despite differences in criteria used to judge functional progression, eyes with standard automated perimetry progression have significantly greater rates of RNFL loss measured using OCT compared with non progressing eyes.

According to Hae young L.park et al,the RNFL area index showed strong correlation with circumpapillary RNFL thickness in perimetric glaucoma

group.However in preperimetric glaucoma ,the correlation strength between RNFL area index and circumpapiilary RNFL thickness was weak. Early in the stage of preperimetric glaucoma, RNFL thickness decreases without apparent decrease in retinal sensitivity by VF. Neverthless, decrease in RNFL area index accompanies changes in retinal sensitivity in the early stage of preperimetric glaucoma, and the structure-function relationships are stronger with RNFL area index than RNFL thickness in preperimetric glaucoma.

[12]Bowd et al reported strongest associations between the inferotemporal RNFL thickness and superonasal visual field sectors using time-domain OCT and scanning laser polarimetry.

Miglior et al also reported stronger associations for the inferotemporal RNFL thickness and its corresponding visual field loss using earlier versions of OCT.These results are in accordance to histological studies and the expected pattern of glaucomatous damage.

[14]Hood et al also proposed a linear model to predict structure –function relationship.

Mauro.T.Leite et al demonstrated that RNFL thinning measured by the cirrus was associated with visual field loss measured by the SAP.In addition they

demonstrated that the shape of relationship changes with scaling of the measurements.

Dimitrios Bizios et al showed that the combination and fusion of data from OCT and SAP has the potential to increase the accuracy of glaucoma diagnostics compared to parameters from either instrument alone.Moreover fusion of test measurements that better reflex both the structural and functional glaucomatous changes that occur during the course of the disease providing more relevant information to glaucoma diagnostic systems.

[8]Andrew J.Tatham et al demonstrated there is growing evidence that early detection of glaucoma is important, particularly, as quality of life may be adversely with even mild loss of the visual field. A major challenge is how best to integrate information from structural and functional tests. The combined structure function index offers a possible solution to this problem and there is emerging evidence that the combined structure functional index is better able to detect glaucoma than isolated measures of structure and function.

OBJECTIVE/AIM

To evaluate correlation between visual field parameters and retinal nerve fiber thickness, optic nerve head changes in 50 cases of glaucoma.

REASON FOR THE STUDY

To evaluate correlation between structure and function of the visual field to aid in the early diagnosis of glaucoma and to prevent progression of glaucoma. The visual field function is established with octopus 301 and the structure of RNFL and ONH is done with SDOCT-SLO.

MATERIAL AND METHODS

This study was carried out at glaucoma clinic, RIOGOH, Chennai, during the period 2013 – 2015.

PROCEDURE

Patient reporting to glaucoma clinic were registered in the glaucoma clinic, RIOGOH, Chennai during the period of 2013 -2015.The study strictly adheres the regulations of the 'INSTITUTION OF ETHICAL CLEARANCE'. Informed consent was obtained from all the participants. Each participant underwent a complete ophthalmologic examination including visual acuity,

refraction, tension by applanation tonometry, anterior segment evaluation by slit lamp biomicroscopy, gonioscopy by goldmann's single mirror indirect gonioscope, fundus examination, visual field by octopus perimetry, optical coherence tomography by SDOCT-SLO and the results are documented for correlative study.

INCLUSION CRITERIA

Primary open angle glaucoma and glaucoma suspects

EXCLUSION CRITERIA

Patient with significant media opacity,

Best corrected visual acuity worse than 6/24,

A spherical correction > + /-5.0D, cylinder correction >+/-2.0D,

History of any retinal disease including diabetic or hypertensive retinopathy ,

History of any eye trauma or surgery with the exemption of any uncomplicated cataract surgery,

History of any surgical or neurologic field that affect the visual field,

Unreliable visual field [false positive> 33%, false negative>33%],

Poor quality OCT images.

ASSESMENT OF PARAMETERS

Visual field parameters by standard automated perimetry is correlated with retinal nerve fiber layer thickness and optic nerve head parameters by SDOCT-SLO in case of primary open angle glaucoma and glaucoma suspects.

RESULTS

Statistical analysis plan - Analysis of data

To analyse the clinical profile of the patient.

To document the best corrected visual acuity.

Assessment of intraocular pressure and Gonioscope.

Assessment of visual field by standard automated perimetry. Assessment of retinal nerve fiber thickness and optic nerve head parameters by SDOCT-SLO.

ANALYSIS AND DISCUSSION

STATISTICAL TOOLS

The information collected regarding all the selected cases were recorded in a Master Chart.

Data analysis was done with the help of computer using **Epidemiological Information Package (EPI 2010)** developed by Centre for Disease Control, Atlanta.

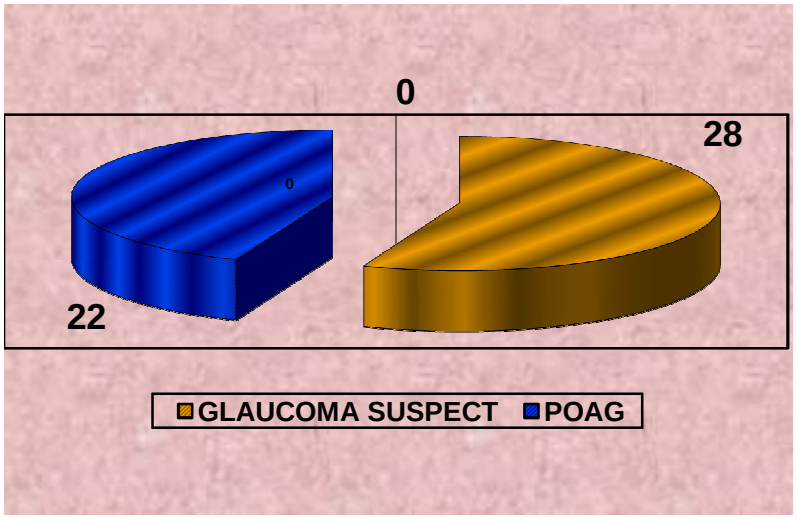
Using this software range, frequencies, percentages, means, standard deviations, chi square, ‘t’ value and 'p' values were calculated.

‘t’ test was used to test the significance of difference between quantitative variables and Yate’s and Fisher’s chi square tests for qualitative variables.

A 'p' value less than 0.05 is taken to denote significant relationship.

Pearson’s correlation coefficient was calculated using Excel software. An ‘r’ value more than 0.5 or less than - 0.5 denotes correlation or association between the two variables.

Table 1 : NUMBER OF EYES INCLUDED IN THE STUDY



Group	Cases	
	No	%
Glaucoma Suspect	28	56
POAG	22	44
Total	**50**	**100**

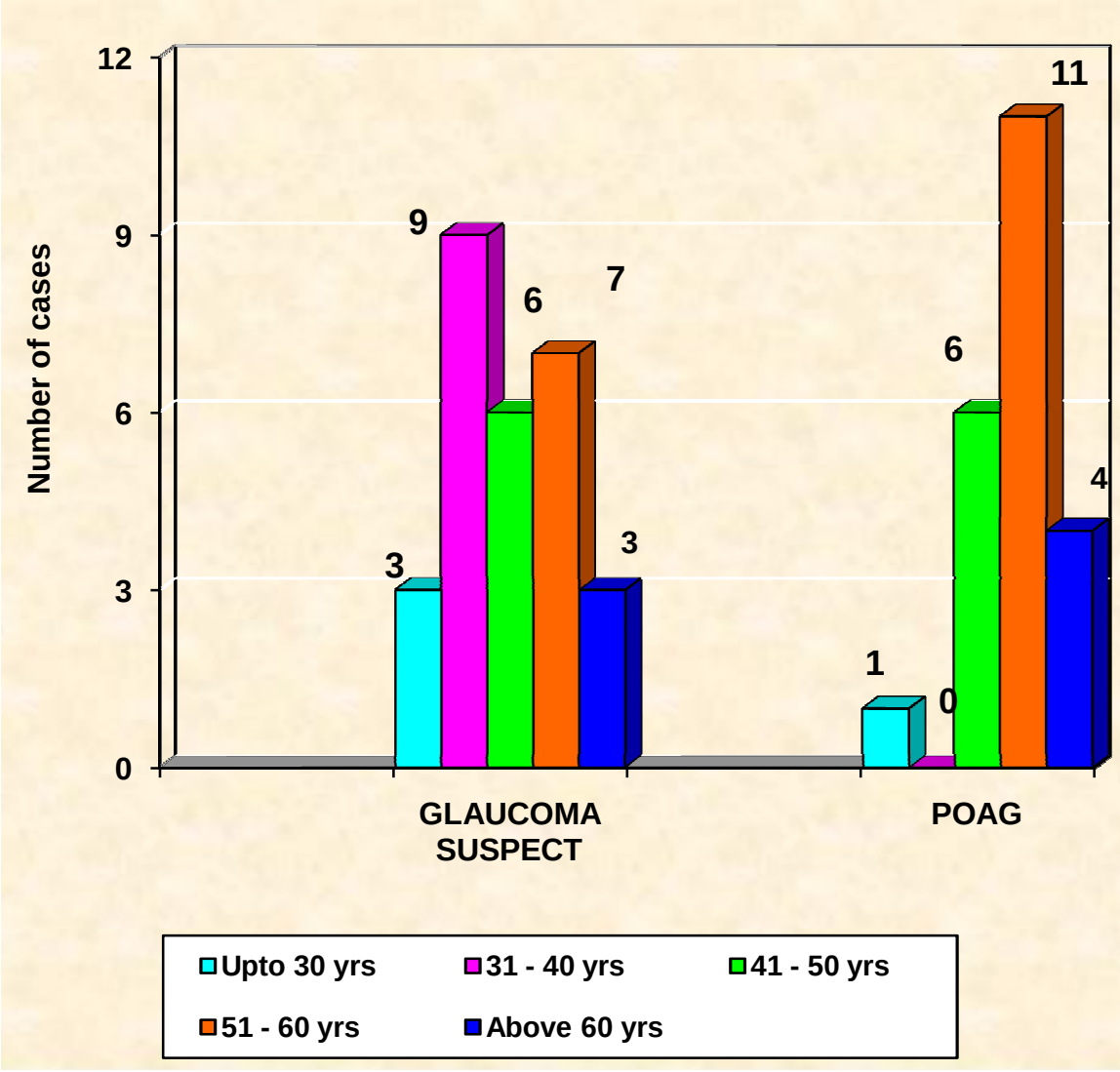
The clinical study consists of admixture of glaucoma suspects and primary open angle glaucoma group. 100 eyes of 50 subjects were taken for the study, of which 56 eyes of 28 patients were categorized into glaucoma suspect group and 44 eyes of 22 patients were categorized into primary open angle glaucoma group.

Table 2 : AGE DISTRIBUTION AMONG STUDY GROUPS

Age Group	Glaucoma Suspect Group		POAG Group	
	No	%	No	%
Up to 30 yrs	3	10.7	1	4.5
31 – 40 yrs	9	32.1	-	-
41 – 50 yrs	6	21.4	6	27.3
51 – 60 yrs	7	25.0	11	50.0
Above 60 yrs	3	10.7	4	18.2
Total	**28**	**100**	**22**	**100**
Range	**22 – 65 yrs**		**21 – 83 yrs**	
Mean	**44.9 yrs**		**54.9 yrs**	
SD	**11.9 yrs**		**12.7 yrs**	
'p'	**0.0063 Significant**			

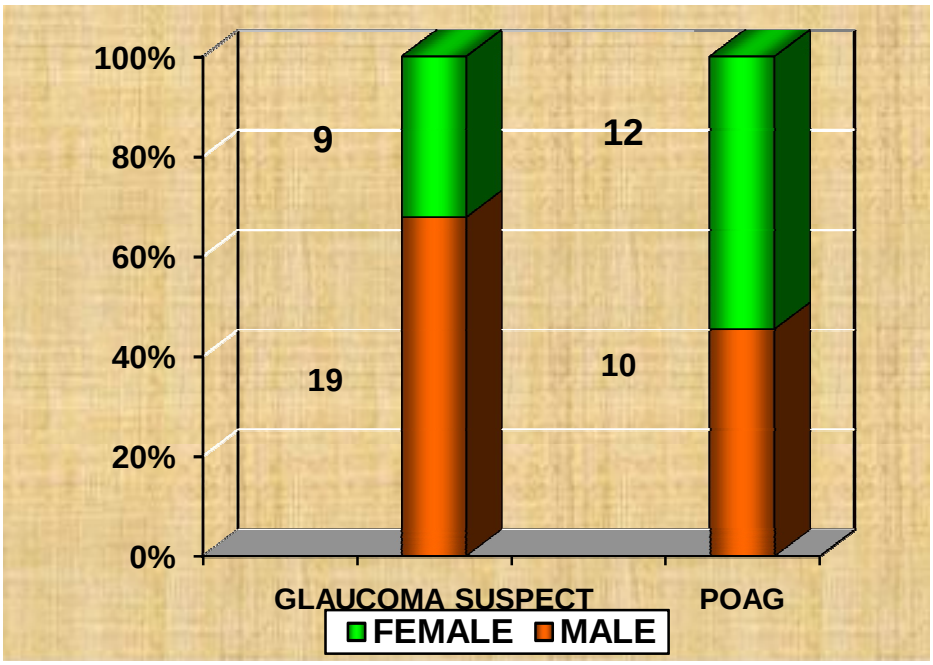
The age distribution of the subjects in the glaucoma suspect group was in the range of 22-65 years with the mean age of 44.9 years and standard deviation of 11.9 years.

The age distribution of the subjects in the primary open angle group was in the range of 21-83 years with the mean age of 54.9 years and standard deviation of 12.7 years.



AGE DISTRIBUTION

Table 3 : SEX DISTRIBUTION



Sex	Glaucoma Suspect Group		POAG Group	
	No	%	No	%
Male	19	67.9	10	45.5
Female	9	32.1	12	54.5
'p'	**0.096 Not Significant**			

The ratio of males to females in the glaucoma suspect group was 2.1:1 with the male predominance.

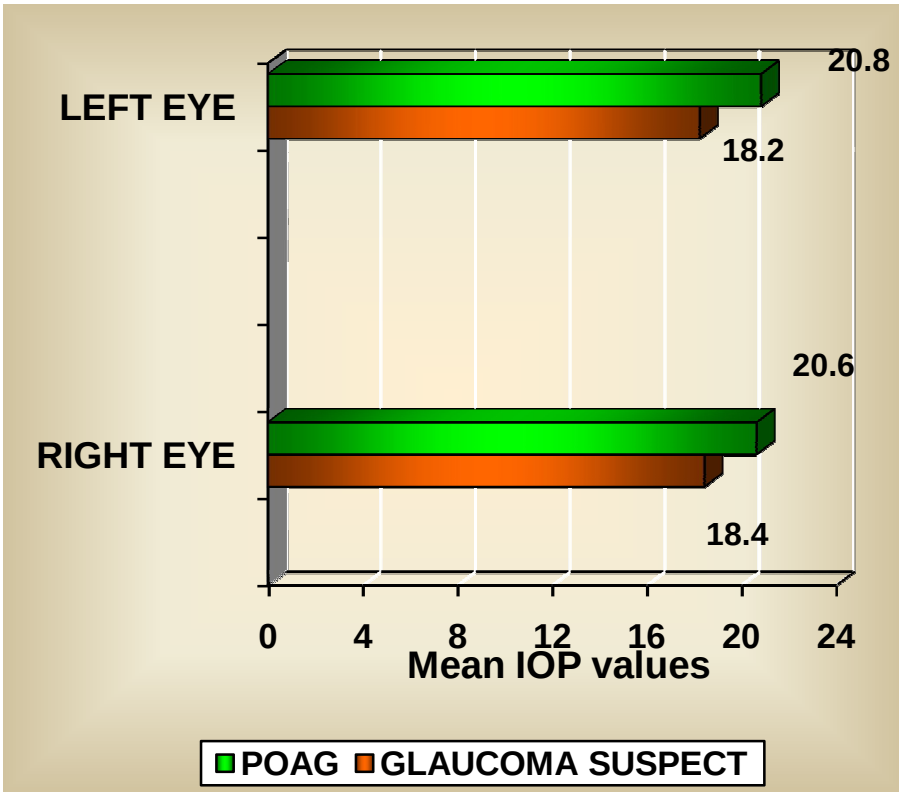
The ratio of males to females in the primary open angle group was 0.83:1 with the slightly female predominance.

Table 4 : RANGE OF BEST CORRECTED VISUAL ACUITY

Visual Acuity	Right Eye				Left Eye			
	Glaucoma Suspect Group		POAG Group		Glaucoma Suspect Group		POAG Group	
	No	%	No	%	No	%	No	%
6/6	16	57.1	10	45.5	18	64.3	9	40.9
6/6P	3	10.7	5	22.7	3	10.7	5	22.7
6/9	4	14.3	6	27.3	2	7.1	4	18.2
6/9P	2	7.1	-	-	1	3.6	2	9.1
6/12	3	10.7	-	-	1	3.6	1	4.5
6/18	-	-	-	-	2	7.1	-	-
6/18P	-	-	-	-	1	3.6	-	-
6/24	-	-	1	4.5	-	-	1	4.5
Total	28	100	22	100	28	100	22	100

The range of best corrected visual acuity ranges from 6/6 to 6/24 in the glaucoma suspects and primary open angle glaucoma group.Poor visual function produces generalized depression of the retinal sensitivity.

Table 5 : INTRAOCULAR PRESSURE AMONG STUDY GROUPS



Intra Ocular Pressure	Right Eye		Left Eye	
	Glaucoma Suspect Group	POAG Group	Glaucoma Suspect Group	POAG Group
Range	10 - 30	16 - 28	12 - 28	14 – 34
Mean	18.4	20.6	18.2	20.8
SD	4.2	3.7	3.7	5.5
'p'	**0.0511 Not Significant**		**0.0516 Not Significant**	

The CCT corrected IOP in the right eye of glaucoma suspect group was in the range of 10-30 with the mean IOP of 18.4 and standard deviation of 4.2.

The CCT corrected IOP in the left eye of glaucoma suspect group was in the range of 12-28 with the mean IOP of 18.2 and standard deviation of 3.7.

The CCT corrected IOP in the right eye of primary open angle glaucoma group was in the range of 16-28 with the mean IOP of 20.6 and standard deviation of 3.7.

The CCT corrected IOP in the left eye of primary open angle glaucoma group was in the range of 14-34 with the mean IOP of 20.8 and standard deviation of 5.5.

CENTRAL CORNEAL THICKNESS

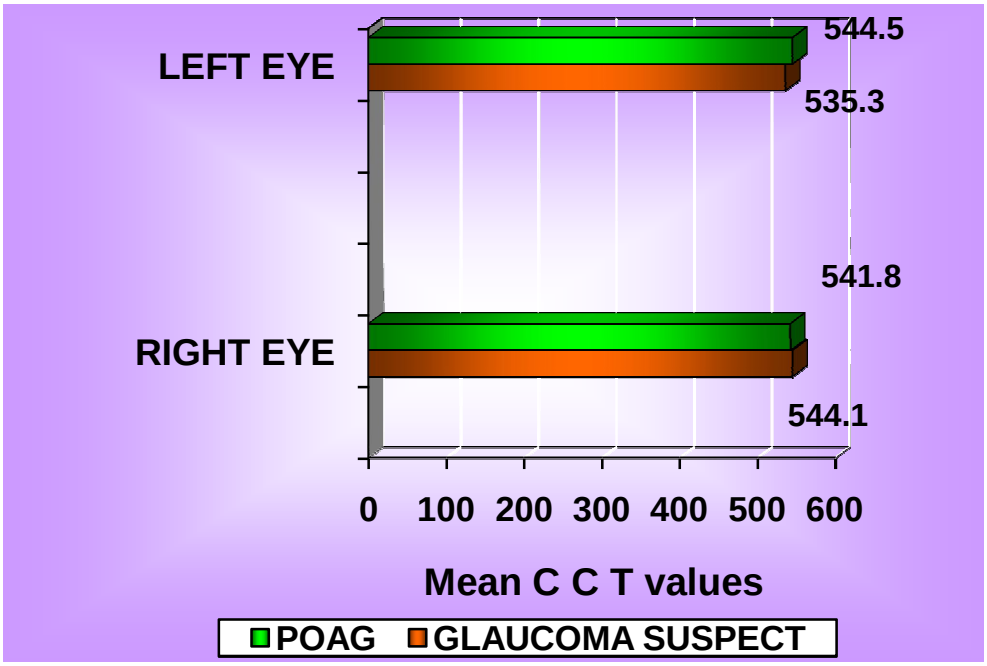


Table 6 : RANGE OF CENTRAL CORNEAL THICKNESS

Central Corneal Thickness	Right Eye		Left Eye	
	Glaucoma Suspect Group	POAG Group	Glaucoma Suspect Group	POAG Group
Range	460 - 607	505 - 603	460 - 608	505 – 604
Mean	544.1	541.8	535.3	544.5
SD	35.7	22.4	39.5	22.7
'p'	**0.7932 Not Significant**		**0.4062 Not Significant**	

The range of CCT in the right eye of glaucoma suspect group was in the range of 460-607 with the mean CCT of 544.1 and standard deviation of 35.7.

The range of CCT in the left eye of glaucoma suspect group was in the range of 460-608 with the mean CCT of 535.3 and standard deviation of 39.5.

The range of CCT in the right eye of primary open angle group was in the range of 505-603 with the mean CCT of 541.8 and standard deviation of 22.4.

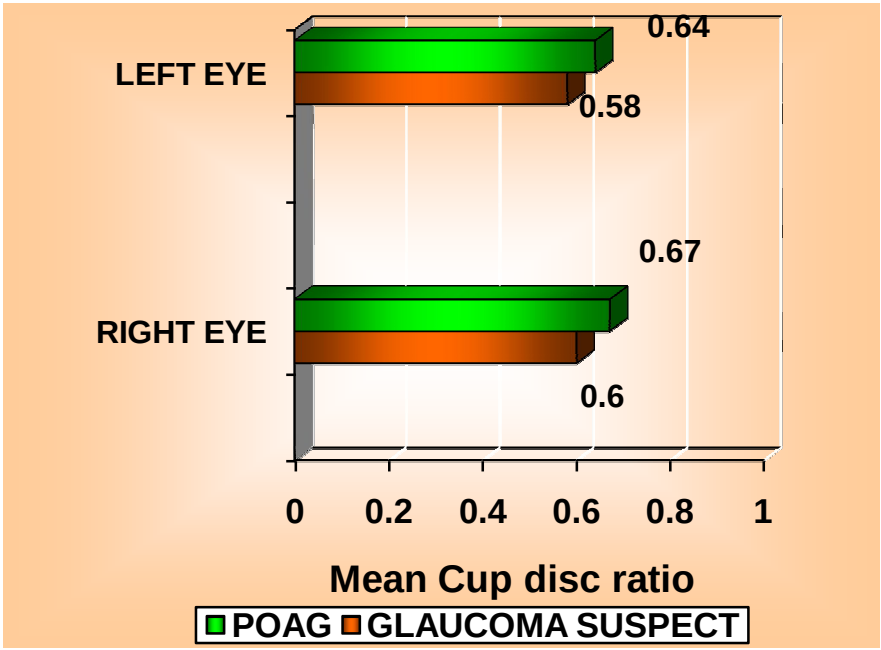
The range of CCT in the left eye of primary open angle group was in the range of 505-604 with the mean CCT of 544.5 and standard deviation of 22.7.

Table 7 : LENS POSITION AMONG STUDY GROUPS

Lens Position	Right Eye				Left Eye			
	Glaucoma Suspect Group		POAG Group		Glaucoma Suspect Group		POAG Group	
	No	%	No	%	No	%	No	%
Clear (NAD)	21	75.0	10	45.4	20	71.4	10	45.4
Lens Changes	3	10.7	8	36.4	4	14.3	9	40.9
Immature Cataract	3	10.7	3	13.6	3	10.7	3	13.6
PC I OL	1	3.6	1	4.6	1	3.6	-	-
Total	28	100	22	100	28	100	22	100

The lens position is indicated since significant media opacities adversely affects the automated perimetry value and interferes with image acquisition in OCT.

Table 8 : FUNDUS (CUP DISC RATIO)



Fundus	Right Eye		Left Eye	
	Glaucoma Suspect Group	POAG Group	Glaucoma Suspect Group	POAG Group
Range	0.3 – 0.8	0.3 – 0.9	0.3 – 0.9	0.3 – 0.9
Mean	0.6	0.67	.58	0.64
SD	0.16	0.15	0.17	0.18
'p'	**0.1271 Not Significant**		**0.2673 Not Significant**	

The range of cup to disc ratio varies from 0.3-0.9 in glaucoma suspects and primary open angle glaucoma group.

The mean cup to disc ratio of the right and left eye of the glaucoma suspects were 0.6 and 0.58 respectively.

The mean cup to disc ratio of the right and left eye of the primary open angle glaucoma group were 0.67 and 0.64 respectively.

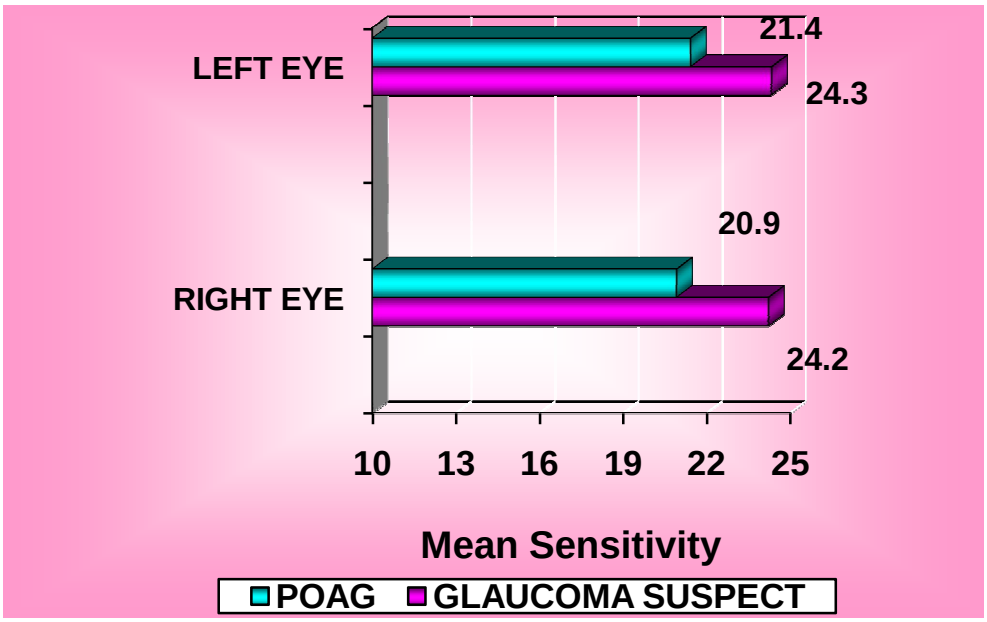
The standard deviation of the right and left eye of the glaucoma suspects were 0.16 and 0.17 respectively.

The standard deviation of the right and left eye of the primary open angle glaucoma group were 0.15 and 0.18 respectively.

AUTOMATED PERIMETER

Table 9 : MEAN SENSITIVITY AMONG STUDY CASES

Mean Sensitivity	Right Eye		Left Eye	
	Glaucoma Suspect Group	POAG Group	Glaucoma Suspect Group	POAG Group
Range	12.9 – 29.3	11.5 – 27	12.7 – 29.8	11.2 – 28.5
Mean	24.2	20.9	24.3	21.4
SD	4.5	5.1	4.6	4.8



Range of Mean Sensitivity

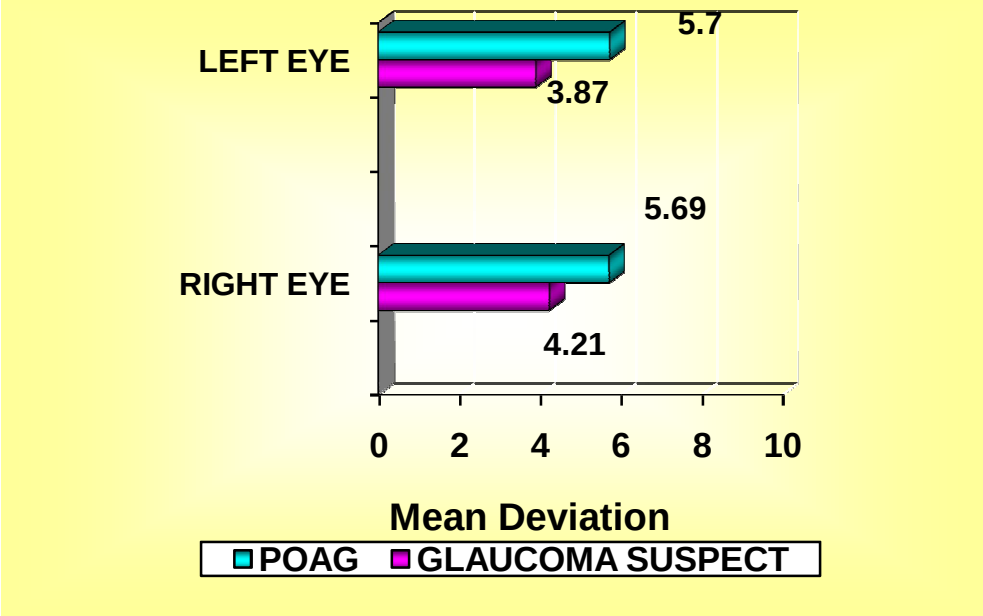
The range of mean sensitivity in the right and left eye of glaucoma suspect group varies between12.7-29.3 and that of primary open angle glaucoma group varies between 11.2-28.5.

The mean in the right and left eye of the glaucoma suspects was 24.2 and 24.3 respectively and that of standard deviation was 4.5 and 4.6 respectively.

The mean in the right and left eye of the primary open angle group was 20.9 and 21.4 respectively and that of standard deviation was 5.1 and 4.8 respectively.

Table 10 : MEAN DEVIATION AMONG STUDY CASES

Mean Deviation	Right Eye		Left Eye	
	Glaucoma Suspect Group	POAG Group	Glaucoma Suspect Group	POAG Group
Range	2.1 – 14.5	0.1 – 16.9	-0.4 – 14.4	-1.3 – 16
Mean	4.21	5.69	3.87	5.7
SD	4.38	5.26	4.48	4.66



Range of Mean Deviation

The range of mean deviation in the in the right and left eye of the glaucoma suspect group was 2.1 to14.5 and -0.4 to 14.4 respectively and that of primary open angle glaucoma group was 0.1 to 16.9 and -1.3 to 16 respectively.

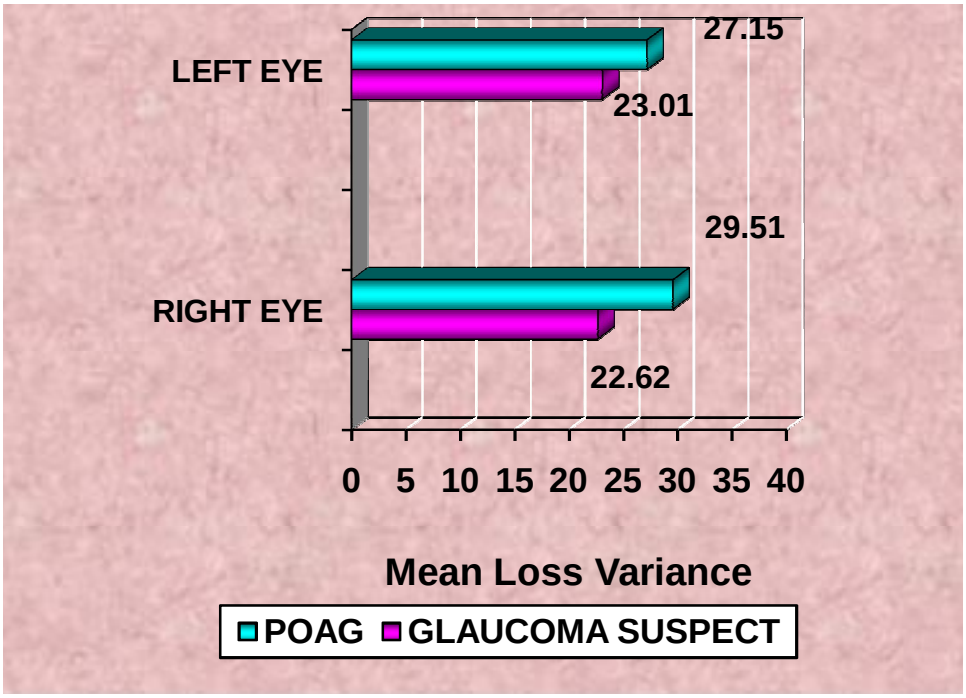
The mean in the right and left eye of the glaucoma suspect group was 4.21 and 3.87 respectively and that of standard deviation was 5.69 and 5.7 respectively.

The mean in the right and left eye of the primary open angle glaucoma group was 5.69 and 5.7 respectively and that of standard deviation was 5.26 and 4.66 respectively.

Table 11 : LOSS VARIANCE AMONG STUDY GROUP

Loss Variance	Right Eye		Left Eye	
	Glaucoma Suspect Group	POAG Group	Glaucoma Suspect Group	POAG Group
Range	1 – 94.5	1.9 – 89.5	0.7 - 137	2.9 – 80.1
Mean	22.62	29.51	23.01	27.15
SD	27.18	25.9	35.53	24.69

The range of loss variance in the right and left eye of the glaucoma suspect group was 1.0 to 94.5 and 0.7 to 137 respectively and that of primary open angle glaucoma group was 1.9 to 89.5 and 2.9 to 80.1 respectively.



Range of Mean Loss Variance

The mean of loss variance in the right and left eye of the glaucoma suspect group was 22.62 and 23.01 respectively and that of standard deviation was 27.18 and 35.53 respectively.

The mean of loss variance in the right and left eye of the primary open angle glaucoma group was 29.51 and 27.15 respectively and that of standard deviation was 25.9 and 24.69 respectively.

Table 12 : RELIABILITY CRITERIA AMONG STUDY GROUP

Reliability Criteria	Right Eye				Left Eye			
	Glaucoma Suspect Group		POAG Group		Glaucoma Suspect Group		POAG Group	
	No	%	No	%	No	%	No	%
a) False Positive								
0%	25	89.3	14	63.6	21	75	16	72.7
25%	1	3.6	4	18.2	1	3.6	2	9.1
33%	2	7.1	4	18.2	6	21.4	4	18.2
b) False Negative								
0%	28	100	21	95.5	28	100	22	100
25%	-	-	1	4.5	-	-	-	-
33%	-	-	-	-	-	-	-	-

The reliability criteria falls under 33% in both the glaucoma suspects and the primary open angle glaucoma groups.

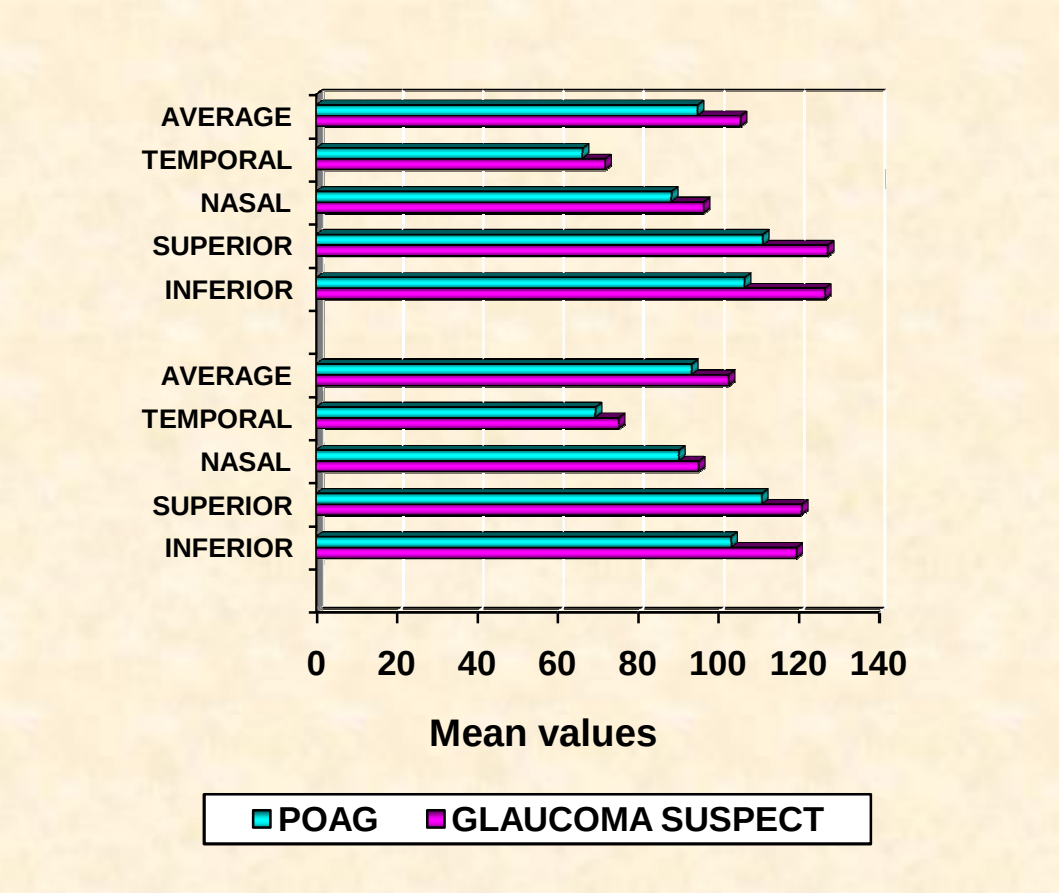
OPTICAL COHERANCE TOMOGRAPHY

Table 13 : OCT RNFL THICKNESS

RNFL Thickness	Right Eye			Left Eye		
	Glaucoma Suspect (Mean ± SD)	**POAG (Mean ± SD)**	**'p'**	**Glaucoma Suspect (Mean ± SD)**	**POAG (Mean ± SD)**	**'p'**
Inferior	119.3 ± 24.0	103.1 ± 25.9	**0.0262 Significant**	126.5 ± 18.3	106.5 ± 22.4	**0.0011 Significant**
Superior	120.6 ± 24.9	110.7 ± 22.9	0.1534 Not Significant	127.1 ± 22.5	111.0 ± 22.1	**0.0147 Significant**
Nasal	94.9 ± 17.6	90.0 ± 19.2	0.362 Not Significant	96.3 ± 17.4	88.2 ± 19.1	0.1235 Not Significant
Temporal	75.1 ± 12.6	69.2 ± 17.0	0.1602 Not Significant	71.7 ± 11.6	66.0 ± 18.4	0.19 Not Significant
Average	102.5 ± 15.9	93.3 ± 17.0	**0.0172 Significant**	105.4 ± 13.3	94.7 ± 17.2	**0.0164 Significant**

The average retinal nerve fiber thickness in the right and left eye of the glaucoma suspect group was 102.5 and 105.4 respectively and that of standard deviation was 15.9 and 13.3 respectively which is significant.

The average retinal nerve fiber thickness in the right and left eye of the primary open angle glaucoma group was 93.3 and 94.7 respectively and that of standard deviation was 17 and 17.2 respectively which is significant.



RNFL Thickness

Table 14 : OCT ONH TOPOGRAPHY

OCT ONH Topography	Right Eye		Left Eye	
	Glaucoma Suspect (Mean ± SD)	POAG (Mean ± SD)	Glaucoma Suspect (Mean ± SD)	POAG (Mean ± SD)
Disc area	3.62 ± 0.84	3.23 ± 0.76	3.64 ± 0.72	3.05 ± 0.84
Cup area	2.32 ± 1.03	2.06 ± 0.78	2.14 ± 1.02	1.77 ± 0.79
Rim Area	1.3 ± 0.49	1.08 ± 0.66	1.46 ± 0.66	1.23 ± 0.86
Cup Disc horizontal	0.82 ± 0.15	0.83 ± 0.11	0.82 ± 0.19	0.83 ± 0.13
Cup Disc Vertical	0.8 ± 0.16	0.85 ± 0.14	0.75 ± 0.17	0.81 ± 0.13
Cup Disc Area	0.64 ± 0.18	0.65 ± 0.19	0.56 ± 0.22	0.58 ± 0.21

Table 15: CORRELATION OF AUTOMETED PERIMATRY AND OCT

Correlation of OCT RNFL Thickness	Right Eye			Left Eye		
	Pearson's Corr. Coefficient with			Pearson's Corr. Coefficient with		
	Mean Sensitivity	Mean Deviation	Loss Variance	Mean Sensitivity	Mean Deviation	Loss Variance
Inferior	0.368	-0.3202	-0.4658	0.3715	-0.3628	-0.2575
Superior	0.2329	-0.2525	-0.3728	0.4575	-0.436	-0.4569
Nasal	0.3445	-0.3322	-0.3982	0.3497	-0.3282	-0.2399
Temporal	0.1982	-0.1522	-0.1729	0.3288	-0.3573	-0.3302
Average	0.3578	-0.3319	-0.458	0.3937	-0.3825	-0.3553

Pearsons correlation coefficient of RNFL average with mean sensitivity is not significant, According to Hae young L.park et al, early in the stage of preperimetric glaucoma, RNFL thickness decreases without apparent decrease in retinal sensitivity by VF which explains the nonsignificant pearsons correlation coefficient ,otherwise the pearsons correlation coefficient of RNFL

average in mean sensitivity and loss variance is significant which explains the strong strucrure function correlation.

Table 16 : CORRELATION OF RNFL AVERAGE WITH OPTIC DISC PARAMETERS

Optic Disc Parameter	Persons Correlation Coefficient of RNFL average in	
	Right Eye	Left Eye
Disc Area	0.2076	0.344
Cup Area	-0.1356	-0.0658
Rim Area	0.4295	0.4913
Cup Disc Horizontal	-0.3089	-0.2099
Cup Disc Vertical	-0.5985	-0.4355
Cup Disc Area	-0.3644	-0.3298

The pearsons correlation coefficient of RNFL average in the right and left eye with the cup –disc area was -0.3644 and -0.3298 which explains significant correlation of RNFL thinning associated with increased cup disc area.

Table 17 : PEARSONS CORRELATION COEFFICIENT OF RNFL AVERAGE WITH GLOBAL INDICES

Global indices	Pearsons Correlation Coefficient of RNFL average in	
	Right Eye	**Left Eye**
Mean Sensitivity	0.3578	0.3937
Mean Deviation	-0.3319	-0.3825
Loss Variance	-0.458	-0.3553

Pearsons correlation coefficient of RNFL average with mean sensitivity is not significant, According to Hae young L.park et al, early in the stage of preperimetric glaucoma, RNFL thickness decreases without apparent decrease in retinal sensitivity by VF which explains the nonsignificant pearsons correlation coefficient ,otherwise the pearsons correlation coefficient of RNFL average in mean sensitivity and loss variance is significant which explains the strong strucrure function correlation.

SUMMARY:

Structure-function maps have been previously developed in order to understand the relationship between the optic disc morphology and the corresponding visual field defects. In 2000, Garway-Heath et al reported one of the most complete structure-function maps in human eyes. Lately, Lamparter et al described the influence of the variability of normal optic nerve head morphology. The high variability of human RNFL distribution around the opticnerve head and the intertest variability of SAP limit the possibility of obtaining stronger correlations between these tests.

1. The clinical study consists of admixture of glaucoma suspects and primary open angle glaucoma group. 100 eyes of 50 subjects were taken for the study, of which 56 eyes of 28 patients were categorized into glaucoma suspects and 44 eyes of 22 patients were categorized into primary open angle glaucoma group.
2. The mean age was 44.9$\pm$ 11.9 in the glaucoma suspects and 54.9$\pm$12.7 in the primary open angle glaucoma group.
3. The clinical study consists of 67.9% male and 32.1% female in the glaucoma suspect group and 45.5% male, 54.5% female in the primary open angle glaucoma group.

4. The range of best corrected visual acuity ranges from 6/6 to 6/24 in the glaucoma suspects and primary open angle glaucoma group.
5. The CCT corrected IOP in the right eye of glaucoma suspect group was in the range of 10-30 with the mean IOP of 18.4 and standard deviation of 4.2. The CCT corrected IOP in the left eye of glaucoma suspect group was in the range of 12-28 with the mean IOP of 18.2 and standard deviation of 3.7. The CCT corrected IOP in the right eye of primary open angle glaucoma group was in the range of 16-28 with the mean IOP of 20.6 and standard deviation of 3.7.The CCT corrected IOP in the left eye of primary open angle glaucoma group was in the range of 14-34 with the mean IOP of 20.8 and standard deviation of 5.5.
6. The range of CCT in the right eye of glaucoma suspect group was in the range of 460-607 with the mean CCT of 544.1 and standard deviation of 35.7. The range of CCT in the left eye of glaucoma suspect group was in the range of 460-608 with the mean CCT of 535.3 and standard deviation of 39.5. The range of CCT in the right eye of primary open angle group was in the range of 505-603 with the mean CCT of 541.8 and standard deviation of 22.4. The range of CCT in the left eye of primary open angle group was in

the range of 505-604 with the mean CCT of 544.5 and standard deviation of 22.7.

7. The lens position is included in the clinical study since significant media opacities adversely affects the automated perimetry value and interferes with image acquisition in OCT.
8. The range of cup to disc ratio varies from 0.3-0.9 in glaucoma suspects and primary open angle glaucoma group. The mean cup to disc ratio of the right and left eye of the glaucoma suspects were 0.6 and 0.58 respectively and that of standard deviation was 0.16 and 0.17 respectively .The mean cup to disc ratio of the right and left eye of the primary open angle glaucoma group were 0.67 and 0.64 respectively and that of standard deviation of primary open angle glaucoma group was 0.15 and 0.18 respectively.
9. The range of mean sensitivity in the right and left eye of glaucoma suspect group varies between12.7-29.3 and that of primary open angle glaucoma group varies between 11.2-28.5.The mean sensitivity in the right and left eye of the glaucoma suspects was 24.2 and 24.3 respectively and that of standard deviation was 4.5 and 4.6 respectively.The mean in the right and left eye of the primary open angle group was 20.9 and 21.4 respectively and that of standard deviation was 5.1 and 4.8 respectively. The range of mean deviation

in the in the right and left eye of the glaucoma suspect group was 2.1 to14.5 and -0.4 to 14.4 respectively and that of primary open angle glaucoma group was 0.1 to 16.9 and -1.3 to 16 respectively.

10. The mean defect in the right and left eye of the glaucoma suspect group was 4.21 and 3.87 respectively and that of standard deviation was 5.69 and 5.7 respectively. The mean in the right and left eye of the primary open angle glaucoma group was 5.69 and 5.7 respectively and that of standard deviation was 5.26 and 4.66 respectively. The range of loss variance in the right and left eye of the glaucoma suspect group was 1.0 to 94.5 and 0.7 to 137 respectively and that of primary open angle glaucoma group was 1.9 to 89.5 and 2.9 to 80.1 respectively.
11. The mean of loss variance in the right and left eye of the glaucoma suspect group was 22.62 and 23.01 respectively and that of standard deviation was 27.18 and 35.53 respectively.The mean of loss variance in the right and left eye of the primary open angle glaucoma group was 29.51 and 27.15 respectively and that of standard deviation was 25.9 and 24.69 respectively.
12. The reliability criteria falls under 33% in both the glaucoma suspects and the primary open angle glaucoma groups and the OCT images with signal strength of 6 and above6 with good image quality is included in this study.

13. The average retinal nerve fiber thickness in the right and left eye of the glaucoma suspect group was 102.5 and 105.4 respectively and that of standard deviation was 15.9 and 13.3 respectively which is significant.The average retinal nerve fiber thickness in the right and left eye of the primary open angle glaucoma group was 93.3 and 94.7 respectively and that of standard deviation was 17 and 17.2 respectively which is significant.
14. Pearsons correlation coefficient of RNFL average with mean sensitivity is not significant, According to Hae young L.park et al, early in the stage of preperimetric glaucoma, RNFL thickness decreases without apparent decrease in retinal sensitivity by VF which explains the nonsignificant pearsons correlation coefficient, otherwise the pearsons correlation coefficient of RNFL average in mean sensitivity and loss variance is significant which explains the strong strucrure function correlation.
15. The pearsons correlation coefficient of RNFL average in the right and left eye with the cup –disc area was -0.3644 and -0.3298 which explains significant correlation of RNFL thinning associated with increased cup disc area.

CONCLUSION:

In conclusion, the pearson's correlation coefficient 'r' value in this study suggests a strong correlation of the functional measurements of standard automated perimetry with the structural elements of SDOCT-SLO in glaucoma suspects and in the primary open angle glaucoma group.

It is also found out in this study that the best parameter to compare the structure-function relationship in glaucoma is to compare the average retinal nerve fiber layer thickness with the mean defect and the loss variance.

It is also found that combining the structure-function data could potentially enhance the performance of early detection of glaucoma.

The OCT also aids in the early detection of structural loss before the evidence loss of visual field function in the standard automated perimetry.

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PROTOCOL (DETAILED DESCRIPTION)

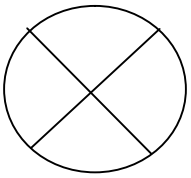
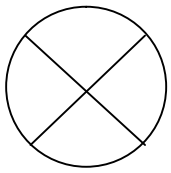
TITLE

"A Correlative study of automated perimetry and optical coherence tomography in glaucoma" at Regional institute of ophthalmology, Madras Medical College & Government General Hospital, Chennai.

NAME	
AGE	
SEX	
OUT PATIENT NUMBER	
GLAUCOMA CLINIC NUMBER	

VISION UCVA	
VISION BCVA	
TENSION BY APPLANATION TONOMETRY	

GONIOSCOPY:

RIGHT EYE	LEFT EYE
	

RELIABILITY INDICES:

AUTOMATED PERIMETRY	
FALSE POSITIVE	
FALSE NEGATIVE	

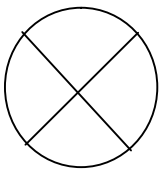
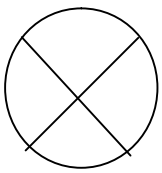
OPTICAL COHERENCE TOMOGRAPHY	
SIGNAL STRENGTH	
Observers grading	

AUTOMATED PERIMETRY

MEAN DEFECT	
LOSS VARIANCE	
SHORT TERM FLUCTUATIONS	
CORRCTED LOSS VARIANCE	
P VALUE	

OPTICAL COHERENCE TOMOGRAPHY

I.RNFL THICKNESS

RIGHT EYE	AVERAGE THICKNESS	LEFT EYE	AVERAGE THICKNESS
			

II.ONH TOMOGRAPHY

DISC AREA	
CUP AREA	
RIM AREA	
C:D HORIZONTAL	
C:D VERTICAL	
C:D AREA RATIO	

KEY TO MASTER CHART:

POAG- Primary Open Angle Glaucoma

BCVA - Best Corrected Visual Acuity

IOP - Intra Ocular Pressure

CCT- Central Corneal Thickness.

AS - Anterior Segment

Gonio - Gonioscopy

MS - Mean Sensitivity

MD- Mean Defect

LV - Loss Variance

FP - False Positive

FN - False Negative

OCT - Optical Coherence Tomography

RNFL - Retinal Nerve Fiber Layer

I - Inferior

S - Superior

N - Naral

T - Temporal

A- Average

ONH - Optic Nerve Head

DA - Disc Area

CA - Cup Area

RA - Rim Area

CDH - Cup Disc - Horizontal

CDV - Cup Disc - Vertical

CDA - Cup Disc Area Ratio

RI - Reliability Indices

AP - Automated Perimetry

SS – Signal Strength

IQ – Image Quality

ABBREVIATIONS:

RGC - Retinal Ganglion Cell

RNFL - Retinal Nerve Fiber Layer

LGB - Lateral Geniculate Body

SWAP - Short Wavelength Automated Perimetry

ATP - Adenosine Tri Phosphate

IOP - Intra Ocular Pressure

MMP - Matrix Metallo Proteinase

BDNF - Brain Derived Natriuretic Factor

TNF - α - Tissue Necrosis Factor - α

IL - I - Inter Leukin – I

i No - Inducible Nitric Oxide

dB - Decibel

AP - Automated Perimetry

OCT - Optical Coherence Tomography

SD - OCT - Spectral Domain OCT

TD - OCT – Time Domain OCT

RPE - Retinal Pigment Epithelium

ILM - Internal Limiting Membrane

C:D Ratio - Cup – Disc Ratio